THE BRITISH JOURNAL
OF
OPHTHALMOLOGY
SEPTEMBER, 1936

COMMUNICATIONS

SOME EFFECTS OF GAMMA RADIATION ON THE DEVELOPING RAT RETINA*

BY

A. GLÜCKSMANN *and* KATHARINE TANSLEY

CAMBRIDGE AND LONDON

Introduction

GAMMA rays from radium even in very small doses have a profound effect on the development of the immature rat retina. Irradiation quickly causes a disturbance of the normal cell division which is followed by widespread degeneration among the undifferentiated cells of the retina, a diminution in the size of the eyeball and the formation of typical retinal rosettes. A new fibre layer dividing the inner nuclear layer may also appear if the retina is subjected to the radiation at a particular stage of development.

The present paper is primarily concerned with the production of rosettes and of the new fibre layer. Although perhaps the most striking result of radiation, these new formations are probably the least fundamental of the effects observed, in that they are only the consequence of an extensive degeneration of cells. The underlying processes which concern alterations in cell division and the production of cell degeneration will be dealt with in a later publication.

* From the Strangeways Research Laboratory, Cambridge, and the Department of Physiology, University College, London.

PREVIOUS WORK.

Rosettes consist of complicated infoldings of the outer part of the retina so that their lumina are bounded by the external limiting membrane through which project the rods and cones. Their appearance is essentially a feature of the developing retina and they only occur in eyes in which there has been some interference with normal development of the immature retina. They are always found in tissue cultures of the retina and can be produced by trephining the undeveloped eye. They are also a well-known feature in glioma retinae (Flexner, 1891; Wintersteiner, 1897). In a previous paper by one of us (Tansley, 1933) the formation of rosettes was discussed in relation to intra-ocular pressure and on the evidence then available it seemed probable that there was some relationship between them.

Rosettes have several times been observed in the retinae of human foetuses which have been aborted after irradiation of the pregnant uterus by X-rays (Goldstein and Wexlar, 1931; Lindenfeld, 1931). They have also been produced experimentally in the rabbit by both X-ray and radium treatment "in utero" (Law, 1934; Pagenstecher, 1916) and in the newborn cat and dog by subjecting the head to X-rays (Demel, 1936; Desjardins, 1931; Tribondeau and Belley, 1907; *a* and *b*, Tribondeau and Récamier, 1905).

The appearance of rosettes in the retina after irradiation was explained by Fuchs, in the discussion on Pagenstecher's paper, as an increased growth of the outer nuclear layer and by Desjardins as due to an inhibition of the growth of the inner nuclear layer. Neither suggestion has any experimental evidence to support it and still leaves unexplained the occurrence of rosettes in unirradiated eyes where a lowering of pressure during development seems to be the important factor. On the other hand there is no evidence that short exposure of the eye to gamma and X-rays has any effect on the intra-ocular pressure.

The experiments to be described here were undertaken in an attempt to discover the precise effect of radiation on the developing retina. Gamma rays were chosen for the irradiation because accurate data on some of the biological effects of given doses were available (Spear, 1935) together with the apparatus with which these data were collected.

METHOD.

Rats were selected for the investigation because the rat retina is not fully developed at birth. Individual animals can therefore be irradiated with precision and then be returned to the mother until required for histological examination. Serial experiments were done on 2-day old rats, and the left eye of each animal irradiated

and then examined. A few rats of other ages up to 11 days were exposed and examined for purposes of comparison.

The source of radiation was 302·1 mgm. radium element, in the form of sulphate, put up in a cylindrical container, 13 mm. in diameter and 2·5 mm. deep. This was mounted for ease of manipulation in a flattened brass ring to form a plaque 4·75 cm. in diameter. The total filtration was 0·5 mm. platinum plus a thin sheet of mica and the distance between the plaque and the eye (left) was about 0·75 cms. The eye thus received only γ rays at an intensity on the skin surface of approximately 280 Sievert units.* The exposures varied from 2 minutes up to 60 minutes, the smallest dose used (2×280 Sievert-minutes) being of the order of 1/33 of the human skin erythema dose.

The technique of exposure was as follows:—a litter of rats with their mother was brought in a cage to the radium room and one of the litter removed and killed as a control. The remaining young rats were then exposed in turn, each being suitably marked for purposes of subsequent identification. To restrict movement during irradiation the rat was wrapped in a blanket of cotton wool and then placed on its right side with its head on a pillow in a wooden cradle fitted with a heating device to prevent any chilling during the radiation. A sheet of mica, mounted on a stand, was then fixed over the cradle so that cross-lines marked on the mica lay over the centre of the left eye of the rat. The mica exercised a very slight pressure on the closed eyelids. The radium plaque, also centred with respect to the mica cross-lines, was then placed in position by hand and the exposure timed by stop-watch. After exposure the rats were returned to their mother and killed at intervals which varied from 20 minutes to 21 days. The left (irradiated) eye of each rat was fixed in Bouin's solution, sectioned and stained with haematoxylin and eosin. Some of the eyes were stained with de Castro's modification of Cajal's silver impregnation method to determine the nature of the new fibre layer which was formed.

Control rats subjected to the same pressure under the mica sheet but without radiation showed no recognisable changes in the eye.

RESULTS.

Fig. 1 shows a section of the normal rat retina 2 days after birth. It will be seen that the optic nerve fibres, the ganglion cell layer, and the inner fibre layer are clearly differentiated. Fixation in Flemming's solution without the acetic acid (F.W.A.) shows that

* One Sievert unit, or intensity millicurie (Imc.), is defined as the intensity due to a point source of 1 mgm. radium acting at a distance of 1 cm.; the rays being filtered through 0·5 mm. platinum.

the inner part of the inner nuclear layer is also differentiated at this age (Fig. 2).

The first recognisable effect of radiation was the diminution of cell division in the retina. This was observed as soon as 30 minutes after the end of a 2-minute exposure with a 2-day rat. If the dose was sufficient mitosis disappeared altogether but later on it returned and sometimes (*i.e.*, with exposures not exceeding 10 minutes) exceeded the normal. This wave of mitotic activity was accompanied by widespread cell degeneration scattered throughout but strictly limited to the outer, undifferentiated, part of the retina. For this reason degeneration was more marked in the periphery of those retinae in which the central parts were already undergoing differentiation. A dose sufficient to destroy practically the whole of the outer part of the retina (30 minutes' exposure on a 2-day rat) was not able to affect those parts which were already differentiated at the time of radiation.

The younger the rat, the greater was the amount of degeneration seen after any given dose. An irradiation of 30 minutes destroyed nearly 90 per cent. of the undifferentiated cells in a 2-day rat but caused no degeneration in an 11-day rat. Table I shows, for 2-day rats, the relation between the amount of degeneration and the dose given.

TABLE I

Showing the relation between the dose of irradiation and the amount of degeneration in 2-day rats.

Duration of exposure in minutes (t)	Intensity of irradiation in Sievert units (I)	Dose ($Ixt.$) in Sievert minutes	Highest count of degenerate cells expressed as per cent. of total undifferentiated cells	
2	280	560	13	—
4	280	1120	25	Maximum reached in 12 hours
6	280	1680	35	—
10	280	2800	43	Maximum reached in 15 hours
12	280	3360	47	—
30	280	8400	89	Maximum reached in 39 hours

The degenerate cells were not scattered indiscriminately throughout the nuclear layers but tended to aggregate in columns between which lay apparently unaffected cells. The direction of these degenerate columns was at first radially, across the retina, but later their position changed so that they formed a band of degeneration within the inner nuclear layer at the junction of differentiated and undifferentiated cells. In this new position the alternation of normal and degenerate cells was still evident. Resorption of the degenerate cells followed and was associated with

(1) a decrease in the size of the whole eye;
(2) the appearance of a new nerve fibre layer on the inner side of the degenerate band;
(3) the formation of rosettes on the outer side of the degenerate band.

(1) *Size of the eye.*—The left eye was always smaller than the right which was further from the radium and never received anything but a very small dose of radiation. Even two months after exposure this difference in size was quite noticeable (12 min. exposure to 280 Sievert units of intensity). The gross appearance showed the diminution in size to the naked eye. Microscopically the retina of the left eye was about the same thickness as that of the other and the number of ganglion and inner nuclear cells was practically equal on both sides but with this dose the visual cells in the left eye were reduced in number by about one-third as compared with the right eye.

(2) *The new fibre layer.*—The new fibre layer was obtained only if the retina was irradiated between 2 and 5 days after birth. When such rats were exposed to γ rays for *10 minutes* or longer a new layer was found splitting the inner nuclear layer into two and separating the differentiated from the undifferentiated cells of this layer. This new fibre layer was fully developed about 3 days (72 hours) after radiation but a few fibres could often be detected as early as 24 hours after exposure.

An exposure of *6 minutes* was followed by the appearance of a few fibres splitting the inner nuclear layer in the extreme periphery of the eye but this effect was only transitory.

Examination of a series of eyes of 2-day rats killed at intervals after a *12 minute exposure* (to an intensity of 280 Sievert units) showed the sequence of events leading to the appearance of the new layer.*

*The normal migration of cells connected with the process of differentiation may be briefly summarised here. Up to the fifth day after birth there is great mitotic activity on the outer edge of the retina. The newly formed cells first migrate inwards. With the decrease of mitotic activity from the fifth day onwards there is an active migration of undifferentiated cells in the reverse direction from the inner to the outer nuclear layer accompanied by increase in thickness of the outer layer.

Twelve hours after exposure degeneration was widely scattered throughout the outer undifferentiated part of the retina (Fig. 3 and Diagram *c*). The tendency of degenerate cells to appear in columns was noticeable. About 24 hours after irradiation the recovery of cell division on the outer edge of the retina combined with the normal inward movement of cells caused a localisation of the necrotic cells in a band separating the outer, undifferentiated, from the inner, differentiated retina. (Fig. 4 and Diagram *d*.) Among the necrotic areas some unaffected cells were seen. Later the dead cells disappeared and their place was taken by a network of fibres which formed a new layer running horizontally along in the inner nuclear layer. This new fibre layer could be easily recognised 72 hours after the application of radium. (Fig. 5 and Diagram *g*.)

If rats whose retinae contained this additional fibre layer were allowed to live for 18 days after the exposure before their eyes were examined it was found that there had been partial fusion of the new layer with the (normal) inner fibre layer. At the same time the inner part of the inner nuclear layer, though still present, was reduced to a single row of nuclei (Fig. 6). In still older eyes the fusion of the two fibre layers was more marked.

An exposure of *30 minutes* destroyed so much of the outer retina that the whole histological picture was for a time completely distorted. Twenty-seven hours after irradiation practically the whole of the undifferentiated part of the retina appeared to be necrotic. Groups of unaffected cells were preserved like islands in the necrotic mass. In places the degeneration extended from the outer edge of the retina to the margin of the differentiated zone. At this margin a fine network of fibres could be detected adjacent to the irregularly arranged inner nuclear cells. A very few degenerate cells were seen in the cavity between the retina and pigment epithelium. The degenerate cells were resorbed by the epithelial cells in the vicinity.

Thirty-two hours after exposure (Fig. 7) great numbers of degenerate cells lay in this cavity. On the outer edge of the retina alternating groups of normal and degenerate cells were seen, while large, round epithelial cells filled with degenerate material were found near to the differentiated parts of the retina and in the cavity outside. The groups of intact cells of the outer retina linked up with the cells of the differentiated area. The network of fibres of the new layer was now slightly more pronounced.

Forty-eight hours after exposure nearly all the degenerate cells had passed into the cavity between the retina and pigment epithelium with consequent contraction of the undifferentiated zone. The fibre network was now very apparent as well as the alternations of intact and degenerate cells. Some of the large, round epithelial cells were free of inclusions, others were still full of them. The pigment epithelium also showed many inclusions.

Seventy-two hours after exposure only a few degenerate cells were present but the retina was considerably thinner than normal, due mainly to diminution in width of the outer nuclear layer and of the undifferentiated part of the inner nuclear layer. The outer nuclear layer was now "arched" (early stage of rosette formation) and where the arches met, the inner nuclear layer formed the outer edge of the retina. The large round epithelial cells were quite free from inclusions. The inner nuclear layer was definitely split into two zones by the new fibre layer.

Treatment of the eyes by silver impregnation showed that the new fibre layer consisted of nervous elements of the same nature as the normal inner fibre layer. There were found:

(*a*) Descending processes of the inner nuclear cells (outer zone) which connected with the ascending processes of the ganglion cells (Fig. 8). The descending processes of the inner nuclear cells (inner zone) were normal.

(*b*) Ascending processes of the inner nuclear cells (inner zone) which made contact with the descending processes of the visual cells in the outer fibre layer.

TABLE II

Showing the relation between effective dosage for producing rosettes and the age of the retina exposed to radiation.

Duration of exposure in minutes*	AGE OF RAT IN DAYS							
	2	5	6	7	8	9	10	11
10	0	—	—	—	—	—	—	—
12	+ + in ciliary region only	—	—	0	—	0	—	0
15	—	+ + in ciliary region only	+ + in ciliary region only	—	—	—	—	0
20	—	+ in ciliary region only	—	+ in ciliary region only	—	0	—	—
30	+ + + throughout retina	—	+ + in ciliary region only	—	+ + in ciliary region only	+ in ciliary region only	0	0
60	—	—	—	—	—	—	—	0

* Intensity of 280 Sievert units constant for all exposures.

(*c*) Processes connecting the horizontal cells with others in the same plane (Figs. 9 and 10).

(3) *Rosettes.*—Typical rosettes were observed in many of the irradiated eyes (Fig. 11). These only occurred in eyes under 9 days of age and with exposures of 12 minutes or more. Table II shows the relationship between effective dosage and age of rat exposed. It will be seen that the older the eye the greater is the dose necessary to produce retinal rosettes and that they cannot be obtained in rats over 9 days of age with any exposures of the range used.

In rats of any age between two and nine days where rosettes were found as a result of radiation they were confined to the ciliary area with the smaller doses, but might spread throughout the retina if the dose was large enough. It was usually found that rosettes would appear in some part of the retina if a minimum of about 50 per cent. of the undifferentiated cells were destroyed.

Rosettes were usually first observed about 48 hours after the exposure, but the early stages of their formation might appear as soon as 36 hours with the higher doses, *e.g.*, in a 2-day retina exposed for 30 minutes. (Fig. 7). The stages of their formation appeared to be as follows:

(i) a degeneration of cells in the inner and outer nuclear layers forming columns separated by normal cells.

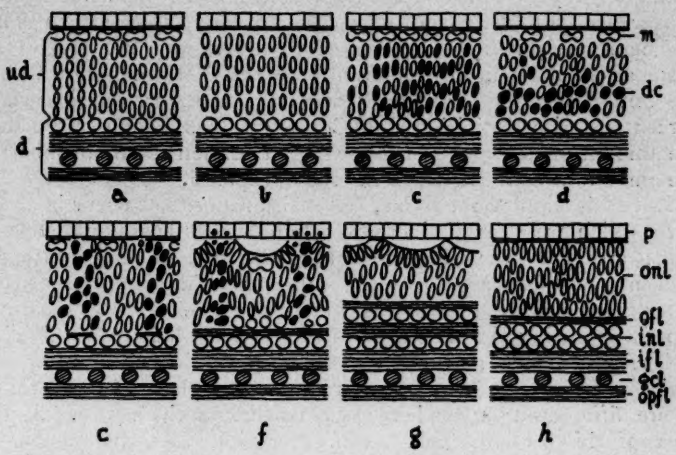
(ii) a breaking of the continuity of the free margin of the retina by the resorption of groups of degenerate cells.

(iii) the tendency of groups of normal cells on free margin of retina to curl up and form typical rosettes.

A number of 5-day old rats, irradiated for 20 minutes at an intensity of 280 Sievert units, were killed and their eyes fixed at daily intervals from one to seven days. At this age the outer fibre layer is already apparent in the central parts of the retina. Twenty-four hours after exposure many degenerate cells were found in the outer part of the inner nuclear layer near the optic disc, while the outer nuclear layer was practically free from them in this region. At the periphery of the eye the outer fibre layer is not yet apparent and here degenerate cells appeared both in the outer part of the inner nuclear layer and in the outer nuclear layer. After 48 hours the degenerations had disappeared except at the periphery of the eye. In some places a fine network of fibres marking the boundary between the differentiated and undifferentiated part of the inner nuclear layer was found, but this disappeared within 24 hours. Rosettes could be seen in all these eyes in the periphery of the retina in the region where degeneration occurred in both outer and inner nuclear layers.

By the fifth day after birth undifferentiated cells are restricted to the outer part of the whole inner nuclear layer, and peripherally to the outer nuclear layer as well. Since irradiation only affects undifferentiated cells it is impossible to reveal a continuous and permanent new fibre layer after this day. On the other hand as a consequence of degeneration in the outer nuclear layer (in the peripheral parts of the retina), rosettes can still be produced here. The differentiation in these parts is sufficiently advanced by the tenth day after birth to prevent any formation of rosettes by irradiation.

DIAGRAMMATIC REPRESENTATION OF NORMAL AND IRRADIATED EYES



(*a*) Normal 2-day rat eye. The optic nerve fibres, ganglion cell layer, inner fibre layer and inner part of the inner nuclear layer are differentiated. Mitosis (*m*) is only found on the outer edge of the retina.

(*b*) Mitotic activity is absent 80 minutes after exposure of gamma rays (12 minutes exposure to 280 Sievert units).

(*c*) 12 hours after exposure to the same dose of gamma rays mitosis has reappeared and degenerate cells (*dc*) are seen in the outer, undifferentiated part of the retina.

(*d*) 24 hours after exposure to the same dose of gamma rays degenerate cells have collected into a necrotic band separating the differentiated from the undifferentiated part of the retina.

(*e*) 36 hours after exposure to the same dose of gamma rays the continuity of the outer edge of the retina has been broken by degenerate cells. The new fibre layer has appeared on the outer margin of the differentiated area (central area of retina).

(*f*) 36 hours after exposure to the same dose of gamma rays degenerate cells have invaded the cavity between retina and pigment epithelium and are being resorbed by the latter. Groups of intact cells on the outer edge of the retina have curled up into rosettes. The new fibre layer is clearly seen (periph ral area of retina).

(*g*) 72 hours after exposure to the same dose of gamma rays degenerate cells have disappeared, the rosettes are being stretched and the continuity of the outer edge of the retina is re-established. The number of inner nuclear cells is normal but that of the outer nuclear cells is reduced. The outer fibre layer is differentiated.

(*h*) Normal 5-day rat eye.

Discussion

The cell degeneration which follows exposure of the developing retina to γ rays is probably the significant factor responsible for the appearance both of the additional fibre layer and of rosettes. This degeneration is, in its turn, related to the mitotic activity of the tissue at the moment of irradiation. (Spear, 1935) has shown that the initial effect of small doses of γ rays is to prevent a certain percentage of cell division and (Cox, 1931) has demonstrated that the amount of degeneration following irradiation is proportional to the amount of cell division in the tissue exposed.

In the developing rat retina, cell division does not occur in those parts which are already differentiated and it has been impossible to detect any histological change in the cells in these areas, with the exposures so far used. On the other hand the undifferentiated outer part of the retina was found to be extremely sensitive, especially during the first 5 days after birth when many dividing cells can be seen along the outer edge of the retina. The number of dividing cells was always greater at the periphery of the retina where differentiation was less advanced than at the centre. As the area of differentiated cells extended peripherally, the number of dividing cells diminished.

After about 6 days from birth, mitosis was found to disappear from the central part of the retina but it persisted to some extent peripherally up to 11 days. The amount of degeneration produced by any given dose of radiation decreased with age and varied with the amount and distribution of mitosis present. Thus, an exposure of 30 minutes caused the death of approximately 90 per cent. of the undifferentiated cells in the central part and completely destroyed the ciliary region of the retina of a 2-day rat, but showed practically no effect on an 11-day retina. The fact that radiation was more destructive to younger eyes would seem to be explained by the relatively greater mitotic activity found in them.

The destruction of undifferentiated cells of the retina by radiation is followed by an aggregation of intact cells to fill the empty spaces caused by the resorption of the degenerate cells. This is accompanied by a renewed mitotic activity. With small doses no apparent disturbance of the normal differentiation is seen. With slightly higher doses a new fibre layer is temporarily formed together with rosettes peripherally. Both rosettes and fibre layer tend to disappear again quickly; the fibre layer by its fusion with the normal inner fibre layer and the rosettes by being stretched into a flattened outer nuclear layer. Only with high doses do these new formations persist for any length of time and even then the tendency is to ultimate disappearance. They are to be considered as transitory steps in the regeneration and organisation of the immature retina

effected in a remarkably short space of time by the neuro- and pigment-epithelium without the aid of vascularisation or connective tissue.

Conclusion

The formation of an additional nerve fibre layer and of rosettes as a result of exposure of the developing retina to γ rays does not appear to be due to any direct effect of the radiation on the tissue but is a sequel to a cellular degeneration which is not specific to radiation.

Summary

(1) A method of exposing the eyes of young rats to γ radiation is described.

(2) One result of radiation is degeneration of the undifferentiated cells of the retina. The amount of degeneration depends on the dose of γ rays and the age of the rat.

(3) The size of the irradiated eye is reduced.

(4) A new fibre layer is formed splitting the inner nuclear layer into two if the radiation is given under appropriate conditions.

(5) Rosettes may also be produced in the retina after γ radiation.

(6) The mechanism of the formation of the new fibre layer and the rosettes is secondary to the degeneration caused by the rays and not a direct effect of radiation.

Acknowledgments.—Our thanks are due to the *British Journal of Ophthalmology*, the Medical Research Council and the British Empire Cancer Campaign for the financial assistance which made the work possible. We are indebted to the Radium Belge in association with Messrs. Watson & Sons for the loan of the radium used. We also wish to thank Mr. C. W. Wilson, physicist to the Strangeways Laboratory, when the work was begun, for designing the apparatus for radiation; Dr. R. J. Lythgoe for taking the photographs from which the figures have been made; and Dr. F. G. Spear for help in preparing the paper for publication.

REFERENCES

Demel, R.—Tierversuche mit der Röntgenbestrahlung des Cerebrum. *Strahlentherapie*, Bd. XXII, p. 333, 1926.

Desjardins, A. U.—Action of Roentgen rays and radium on the eye and ear. *Amer. Jl. Roentgenol.*, Vol. XXVI, pp. 639 and 787. 1931.

Flexner, S.—A peculiar glioma (neuroepithelioma?) of the retina. *Johns Hopkins Hosp. Bull.*, Vol. II, p. 115, 1891.

Cox, S. P.—Sensitivity to X-rays of cells *in vitro*. *Archiv. f. esp. Zellforsch.*, Bd. XI, p. 121, 1931.

Goldstein, I., and Wexlar, D.—Rosette formation in the eyes of irradiated human embryos. *Arch. of Ophthal.*, Vol. V, p. 591, 1931.

Law, F. W.—Ultra-violet therapy in eye disease. London, 1934.

Lindenfeld, B.—Beitrag zur Bildung rosettenartigen Figuren in der Netzhaut sonst normaler fötaler menschlichen Augen. *Klin. Monatsbl. f. Augenheilk.*, Bd. LI, p. 440, 1931.

Pagenstecher, H. E.—Strahlenwirkung auf das fötale Auge; Experimentelle Untersuchungen über die Entstehung der Netzhautrosetten. *Versamml. Ophthal. ges. Heidelberg*, Bd. XL, p. 447, 1916.

Spear, F. G.—Tissue culture and radiological research. *Brit. Jl. Radiol.*, Vol. VIII, pp. 68 and 280, 1935.

Tansley, K.—The formation of rosettes in the rat retina. *Brit. Jl. of Ophthal.*, Vol. XVII, p. 321, 1933.

Tribondeau, L., and Belley, G.—Actions des rayons X sur l'oeil envoi de dévéloppement. *Arch. d'elec. med.*, T. XV, p. 907, 1907.

——— Microphtalmie et modifications concomitantes de la rétine par Röntgénisation de l'oeil d'animaux nouveau-nés. *Compt. rend. Soc. d. Biol.*, T. LXIII, p. 128, 1907.

Tribondeau, L., and Récamier.—Altérations des yeux et du squelette facial d'un chat nouveau-né par Roentgénisation. *Compt. rend. Soc. d. Biol.*, T. LVIII, p. 1031, 1905.

Wintersteiner, H.—Das Neuroepithelioma retinae. Wien, 1897.

EXPLANATION OF FIGURES

FIG. 1.—Section through the eye of a normal 2-day rat. The optic nerve fibres, ganglion cells and inner fibre layer are differentiated. Mitosis is found only on the outer edge of the retina.
(Bouin, Haematoxylin-Eosin H. and E.; ×160.)

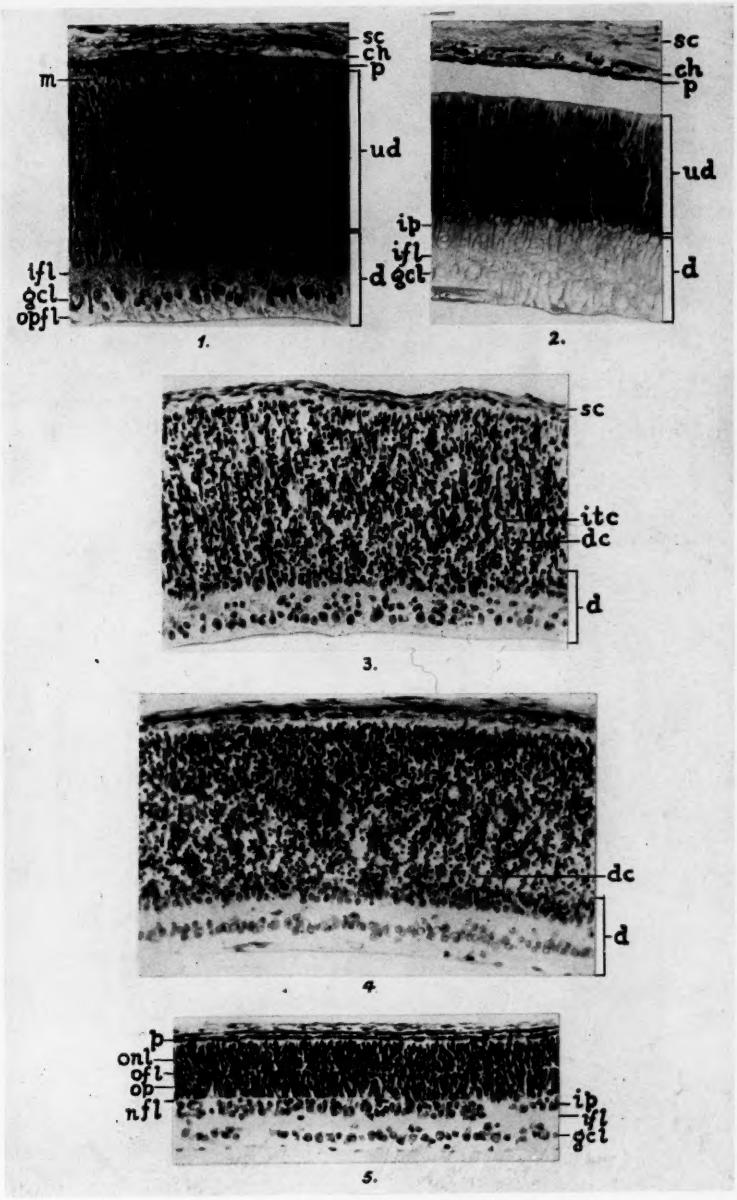
FIG. 2.—Section through the eye of a normal 2-day rat, which was fixed in Flemming's solution without acetic acid. This shows that the inner part of the inner nuclear layer is also differentiated.
(Iron Haematoxylin; ×160.)

FIG. 3.—Section through the eye of a 2½-day rat, 12 hours after exposure to gamma rays (*12 minutes exposure* at 280 Sievert units of intensity) at 2 days old. In the outer undifferentiated part of the retina strands of intact cells (itc) alternate with columns of degenerate cells (dc).
(Bouin, H. and E.; ×160.)

FIG. 4.—Section through the eye of a 3-day rat, 24 hours after exposure to the same dose of gamma rays at 2 days old. The degenerate cells have collected roughly into a band separating the differentiated parts of the retina from the outer, undifferentiated part.
(Bouin, H. and E.; ×160.)

FIG. 5.—Section through the eye of a 5-day rat, 72 hours after exposure to the same dose of gamma rays at 2 days old. The band of degenerate cells has disappeared and its place is taken by a new fibre layer dividing the inner nuclear layer into two parts.
(Bouin, H. and E.; ×160.)

FIG. 6.—Section through the eye of a 20-day rat, 18 days after exposure to the same dose of gamma rays at 2 days old. A thinning of the inner part of the inner nuclear layer is seen together with a partial fusion of the inner fibre layer with the new fibre layer. The outer nuclear layer shows rosettes.
(Bouin, H. and E.; ×160.)


sc
ch
p
m
ud
ifl
gcl
opfl
d
1.
sc
ch
p
ud
ip
ifl
gcl
d
2.
sc
itc
dc
d
3.
dc
d
4.
p
onl
ofl
op
nfl
ip
ifl
gcl
5.

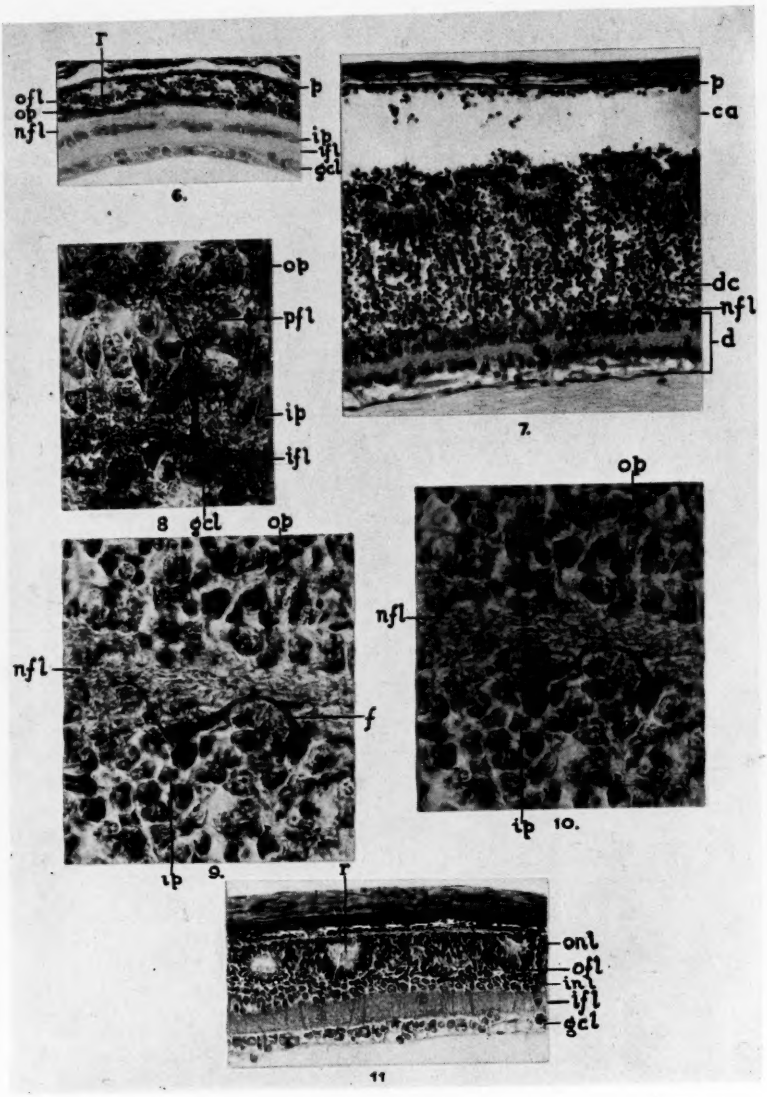

I
ofl
op
nfl
p
ip
ifl
gcl
6.
p
ca
dc
nfl
d
7.
op
pfl
ip
ifl
8
gcl
op
nfl
f
ip
9.
op
nfl
ip
10.
I
onl
ofl
inl
ifl
gcl
11

FIG. 7.—Section through the eye of a 3½-day rat, 32 hours after exposure to gamma rays (*30 minutes exposure* at 280 Sievert units of intensity) at 2 days old. The continuity of the outer edge of the retina is broken by degenerate cells which have also invaded the cavity (ca) between retina and pigment epithelium. Groups of intact cells on the outer edge of the retina have curled up into rosettes and are linked by columns of intact cells with the cells of the differentiated area. At the margin of the differentiated part of the retina the network of fibres of the new fibre layer can be seen.

(Bouin, H. and E ; ×160.)

FIG. 8.—Section through the eye of a 5-day rat, 72 hours after exposure to gamma rays (*12 minutes exposure* at 280 Sievert units of intensity) at 2 days old. An ascending process of a ganglion cell passes through the inner fibre layer and the inner part of the inner nuclear layer and connects, in the new fibre layer, with a descending process of an inner nuclear cell of the outer zone.

(de Castro ; ×650.)

FIG. 9.—Section through the eye of a 5-day rat, 72 hours after exposure to the same dose of gamma rays at 2 days old. In the new fibre layer processes running horizontally connect cells of the inner zone of the inner nuclear layer. Owing to the impossibility of photographing all parts of the fibre in focus simultaneously, this figure has been retouched.

(de Castro ; ×650.)

FIG. 10.—The original photograph of Fig. 9.

FIG. 11.—Section through the eye of a 20-day rat, 18 days after exposure to the same dose of gamma rays at 2 days old. Typical rosettes (r) are seen in the outer nuclear layer.

(Bouin, H. and E. ; ×160.)

ABBREVIATIONS

ca	Cavity between retina and pigment epithelium.	*nfl*	new fibre layer.
ch	choroid.	*ofl*	outer fibre layer.
d	differentiated part of retina.	*opfl*	optic nerve fibres.
dc	degenerate cell.	*op*	outer part of inner nuclear layer.
gcl	ganglion cell layer.	*onl*	outer nuclear layer.
inl	inner nuclear layer.	*p*	pigment epithelium.
ip	inner part of inner nuclear layer.	*r*	rosettes.
itc	intact cell.	*sc*	sclera.
ifl	inner fibre layer.	*ud*	undifferentiated part of retina.
m	mitosis.	*f*	nerve fibre.

INFLAMMATORY DISEASE IN THE EYE CAUSED BY GOUT

BY

D. J. WOOD

CAPE TOWN

IN this twentieth century now one third gone we are apt to forget what a large part was played or was supposed to be played by gout in the days of our great-grandfathers.

Even the older ophthalmic surgeons are, I think, in danger of overlooking gout as a cause or a complication in the production of certain eye diseases, the more so because they are not common. No doubt it is true that many of the ailments formerly ascribed to gout are known now to be due to quite other conditions, but nevertheless in our more limited experience, since gout has become less frequent than it was, we find from time to time cases of ocular disease which correspond exactly with those carefully described by Jonathan Hutchinson, and by him correctly attributed to gout.

With four such cases I have had to deal during the last fifteen years. In them no other gross or manifest evidence of gout existed, and therefore other and more modern aetiologies had been sought, and paid for, without success.

The cases were all more or less similar, and as they are not common and little has been written about them of recent years it may be worth while to give the records in detail.

In all the first sign of trouble was an attack of episcleritis fugax, and this continued to form part of the syndrome through the course of the trouble.

My first case occurred in 1920, when a lady sixty years old came to me complaining of a recent pain in her left eye, which had come on suddenly, and was associated with prominence of the eyeball. The attack had occurred on a Saturday night, and when I saw her on the following Monday it had largely disappeared. There was still conjunctival redness, the eyelids were swollen, and the eye a little proptosed. There was no discharge from the eye, and no implication of the cornea or iris. Pain had ceased but had been severe, and felt all through the orbit. She had coronary cataract, rather extensive, and even the correction of her myopia gave her only 6/24ths of vision.

She had lived in India for some time where her husband's position had made hospitality and good living part of his duties, and subsequently she at least had not fallen behind her former habits. I could not come to a diagnosis, the nearest approach to

my mind being that it had been produced by some external irritant, possibly a pollen, though the dryness of the eye was against this. I did not realise the condition as a danger signal, and owing to my compulsory indefiniteness I did not see her for a long time, as she went to England when her attacks recurred. There she was told she had iritis and various examinations were made to find a septic cause. Curiously her very bad teeth seemed not to have been considered as requiring attention. Examination of the eye when she came back shewed that she had a couple of small iritic adhesions which did not tally with her tale of sixteen severe attacks during the interval since I saw her first. The attacks were always the same. Severe burning pain in the eye, with redness, and more or less protusion of the eyeball. It came on quickly, and lasted as a rule between one and three days during which time she could scarcely open her swollen eyelids, or use her eye in any way. After each attack the eye cleared up rapidly and became as good or nearly as good as formerly. I got her own medical attendant to examine her carefully on the supposition that the attacks were episcleritis periodica fugax, but I had never seen her in one except when it had nearly passed off.

He found very little amiss. She had a subnormal temperature but no other evidence of thyroid insufficiency. There was some arteriosclerosis, and a good deal of increase over normal blood pressure. Her teeth were very bad. These were dealt with radically, and she was put on very light diet with almost nothing in the way of alcohol. For local atacks she was to use atropine and dionine and hot bathing. For a time her attacks lessened. Recurrences induced her however to try elsewhere and she was again treated for iritis and was made rather ill by a protein shock. In the end however I was asked to come to her own home and I saw her for the first time during a bad attack. Her eye was greatly proptosed, the eyelids swollen and red, there was conjunctival redness and chemosis and the iris looked dull with a very small pupil. She could not open the eye, and movement of the other eye gave much pain. She had had no sleep during the night. It was clear that she had episcleritis fugax with other features added probably tenonitis and perhaps iritis. Like former attacks this one passed off in about three days and when I was able to see her in my consulting room there was very little left amiss. Each attack did however leave her a bit worse as regards vision, and she became unable to read. More pupillary adhesions formed, more pigment was deposited on the lens and there were vitreous opacities. Her death from cardiac failure and hypostatic pneumonia ended further observations.

Case 2.—A gentleman aged about 66 came to see me at my residence in 1932 on account of swelling and redness of his left

upper eyelid. The sclerotic was also red, and the conjunctiva oedematous.

His idea was that he had been bitten by a mosquito, and the appearances were by no means unlike such a cause. When however he returned with the same thing in the same eye a few months later I thought that episcleritis periodica fugax was a more likely explanation. Treatment with dionin seemed to end the trouble and I did not then realise as I do now that it might be the precursor of much worse things. A few similar attacks occurred in 1933 but in 1934 he got an attack which during my absence was diagnosed as severe iritis. When I returned and saw him it was clear that he had had iritis, but the only evidence left was a single small iritic adhesion in his right eye. He had been told also that he had pernicious anaemia the diagnosis being based on measurement of his blood cells. I got him carefully examined and it was found that he had a megalocytic anaemia not however of the pernicious type. He had been losing weight, and occasionally there was a trace of blood in his stools, but with no evidence of any malignant disease of his intestinal tract. He had lived well, being a large meat eater, and he had been generous in his allowance of rather heavy wines.

His diet was restricted, and for a long time he was definitely better in health, but before very long he got a second severe inflammatory attack in his right eye. The conjunctiva was oedematous, the iris very dull, and the aqueous extremely hazy.

The uric acid content of his blood during the attack was 4·6 milligrammes per 100 c.c. while in the succeeding interval it was only 3·5 milligrammes. Another symptom which he had had for long was a dry itchy skin which was said to be due to " metabolic disturbances " by a dermatologist.

It was curious that in spite of the alarming looking state of his eye he had hardly any pain, merely discomfort, and indeed throughout all his attacks which went on during over two years he rarely had recourse even to aspirin, though when his eye was uncomfortable during the night this gave him relief and sleep. The attacks were not confined to his right eye but the damage done to it was the greater, and iritic adhesions gradually made it impossible to get more than partial dilation of this pupil. During an attack his aqueous would be filled with a fibrinous coagulum which vanished quickly with the subsidence of the acute stage. The dieting brought for a time an increase in weight and an improvement in his anaemia, but this was not permanent and he got recurring inflammatory attacks in one or other eye. They lasted about a week and were not associated with any proptosis. In March, 1935, his vision had been 6/12 in the right eye, and 6/9 in the left, but by October it was much less in the right, and if

the left eye was inflamed he could not read. In this same month he developed two new conditions, oedema of his eyelids, round the eyes, and back towards his ears, and in his arms, and in his eye attacks he began to get precipitates on the back of his corneae which till then had been absent. Like the rest of his eye inflammation these precipitates disappeared with unusual rapidity when the attack subsided. He continued to grow thinner and for a week went on a Bulgarian milk diet. This did not however help, and he went to another physician for an opinion. It was found that in addition to arterio-sclerosis and enlarged heart he had an extensive venous thrombo-angiitis. His anaemia was severe and a more generous diet had to be allowed.

This brought his blood cells to about half normal and his haemoglobin to 46 per cent. I had tried to get him to go to England for an opinion by someone expert in gouty conditions but he refused. In the end the opinion by his second physician alarmed him, and he decided to go, but to Germany. In this however his heart failure intervened. He became ill soon after his arrival, and died of cerebral haemorrhage.

In contrast to the former case he had no pain, and no proptosis while both these were present in the other. This seemed to associate the pain with Tenonitis, agreeing therefore with observations by Hutchinson that pain is not severe in gouty iritis without other complications. He emphasised the fact that while there might not be much pain, gouty iritis may be insidious and destructive. I think that there is little doubt that had my patient lived long enough he would have become practically blind.

Case 3.—A lady then of forty-six years came to consult me in 1932. Her story was that she had had three attacks of pain in her left eye which had been diagnosed as iritis. She had also had a marginal ulcer of which one could see a faint scar.

I found a single round ball of pigment in the pupillary area, and three specks of pigment lower down where iritic adhesions had probably given way. Her story of very severe pain seemed out of proportion to what one could see amiss, and I thought it might have been an actual fifth nerve neuralgia.

One could see far back in the vitreous some rounded opacities, but her vision was 6/5. She was presumably not satisfied, and I did not hear of her again till April, 1934, when at a University faculty meeting two of the staff independently spoke to me about the case. The description was so clear that one felt nothing except episcleritis periodica fugax with possible complications could explain the attacks.

She was brought back to me and gave a history of much having been done to her. Her teeth had been extracted, her tonsils had been removed, and she had had a gynaecological operation.

She had been given atophan by her own medical attendant, and it was suggested that her liver had thereby suffered. She had in fact had much done both medically and surgically to discover a cause for her frequent attacks of severe ocular pain, and was definitely neurotic in consequence.

Examination shewed little advance since her former visit except that there were now three small synechiae where the former pigment spots were. In the vitreous however were numbers of rather large rounded opacities, larger than the ordinary dust seen in irido cyclitis, and very sharply defined. I have seen such before but have not been able to explain their nature.

The attacks of pain had become very frequent, so that she was hardly ever free for more than a week, and yet her iris was bright and almost free from adhesions. I decided that it was probably gouty and in her next attack her blood was taken and shewed 4·14 milligrams of uric acid per 100 c.c. while between attacks it was 2·3 milligrams. She was put on a diet which she probably adhered to, but she did not take kindly to any drugs. Colchicum upset her digestion, atophan made her itch and I do not know how far she kept on with any medical treatment. In the height of an attack there was eyelid oedema, proptosis, dislike of moving the eyes, iris dullness and great scleral redness which lasted longer than the iris change.

As the patient was confined to bed it was not possible to get a satisfactory examination during the worst stage. In April, 1934, I did get her to come to my consulting rooms just after an acute attack. My attention was drawn to some faint blurs on her cornea which were new, and the slit-lamp shewed them to be acicular crystals in sheaves, narrowed in the middle. They were less than one millimetre in length. Descemet's membrane was also covered with stellate points and dots, whether crystalline or not was uncertain. There was a lot of vitreous haze, and she admitted seeing 6/60 only. I could however see large fundus vessels. One had to admit that the patient was not improving, and I was not surprised to hear that she wished to go to England. I went to the trouble of writing out a long report for a well-known London ophthalmologist, and sent it to him, giving the patient an introductory note. Unfortunately she was diverted elsewhere, so that my record was not available for the gentlemen to whom she went. He agreed however that Tenonitis was present. She came back without any report on her general condition which was what I specially desired, and in place of improvement became gradually much worse.

Morphia and hyoscine had to be given whenever the attacks occurred, and vision was getting progressively worse. There was hardly any fundus reflex and vision of a lighted hand was good

only on the temporal side. In spite of all this however as soon as the pain ceased the iris would become bright again and the original synechiae were all that existed. Finally she agreed to part with the eye, and it was excised under sodium evipan, the socket being very freely washed out with warm alkaline solution. No further trouble has occurred in the socket though of course much of Tenon's capsule was left. She has since had slight scleral redness in her good eye but nothing in the way of episcleritis periodica fugax.

My fourth case has been too satisfactory to be instructive. A man about fifty years of age came to me with a history of repeated acute attacks of pain and redness with protrusion of his right eye. He had seen two ophthalmic surgeons, and he gave me a long list of physicians to whom he had gone. The attacks had been going on for more than a year, and he was just over one when he came to me. There was however enough for a diagnosis to be made. He had been a big meat eater and drank lots of beer. He undertook to change his habits, and I have seen him no more though he has assured me on the telephone that he will come back at once if he gets more trouble. He has been free for nine months from all attacks. Here again his pain seems associated with proptosis, and inferentially with Tenonitis.

Taking the four cases one found that all began with a sudden scleral redness which usually came on during the night, and was not painful, though Hutchinson's term "Hot Eye" described the sensations well enough. Episcleritis periodica fugax is also a good description. It is not a very painful condition when uncomplicated, and till I saw the first of the cases here recorded it had not struck me as being serious, though I admit that few have come my way. Cases have been recorded as occurring in several members of the same family. This can be understood if all inherited or acquired a gouty diathesis.

In the three first cases iritis looked much more severe than would be guessed if one judged by the small residual damage, and this conforms to the appearances seen in sections of the iris. The very sudden onset, relatively short duration, and rapid cessation of pain, are all in contrast to what obtains in the majority of cases of iritis, and suggests that the irritant is not bacterial but possibly chemical. The appearance of severe irido-cyclitis is exaggerated by the lid oedema, but the amount of tenderness to pressure was very slight. Even where there had been exudate into the anterior chamber, and, in my second case, deposits on the endothelium, these cleared up remarkably quickly when the acute stage ended. Vitreous opacities were present in all, and in two were rather large rounded atoms. One was tempted to say they might be urates, but a chemical test gave no support to this. The three cases

which complained of pain all had proptosis, and in two any movement of the eyes made this worse, indications I think of Tenonitis. The corneal crystals were new to me and could not have been seen in pre-slit-lamp days. Mr. Doggart's interesting paper appeared in this Journal just after I saw them, and from it I learned that Weve and Scheffels had seen similar crystals in what they called keratitis urica.

Since it is now possible to get accurate estimates of the uric acid content of the blood we are in a better position to diagnose gout. It would appear to be reliable not so much when there is a mere increase, as when the increase corresponds with the attack of inflammation. South Africa is however not a gouty country, and few medical men have much first-hand experience of it. As the country makes and uses large amounts of rather heavy and often acid wines, the absence of gout may perhaps be due in some way to the absence of the hereditary element.

Treatment to be effective must I think be early, drastic, and suggested with confidence. This point is brought out in Case 4 by its success, and by the comparative failure in the other three. The patient must be left in no doubt as to what is amiss, and he must be made to understand that it is due to a condition which may be hereditary, but which is almost certainly of longer standing than his complaints. Unless he is convinced he will not take kindly to restrictions of diet, and stoppage of alcohol. Further he must be prepared to put up with discomforts produced by medicines, whether colchicum or cincophen. I do not know of any local treatment save dionine, and, when there is iris involvement, atropine. Possibly hyoscine will have to be substituted in many cases owing to the chance of producing atropine irritation. Heat in any form will give some relief. As to pathogenesis we are still waiting for knowledge.

I believe that it is admitted now that uric acid *per se* is not the cause of gouty inflammation in the tissues. A high degree of uric acid content in the blood may be however the first evidence of an abnormality in nuclein katabolism. The excessive amount may be due either to this or to large quantities of nucleins and purin bodies in the diet. The former would supply the hereditary element, the latter the acquired. As a result of a raised kidney threshold for uric acid a uricaemia results. In the tissues the uric acid anions meet with sodium cations forming sodium urate, some of which is excreted and some deposited locally. The loss of sodium cations may however upset the ionic balance both in the cells and the surrounding fluid, and in consequence other cations may become toxic and produce a pathological or destructive action. If this be so, the tissues containing much sodium would be most affected, and it is interesting to note that in the eye those

are the sclerotic, the cornea, and the choroid. The avascularity of the cornea would however save it from serious damage. In the cases described the sclerotic was always the first to suffer, and in some cases it never goes further.

There is a suggestion that the attacks recur as a result of foregoing attacks. Since the eye of Case 3 has been removed, there has been no trouble in the socket, or anywhere else save slight and apparently unimportant redness in the remaining eye, entirely different in character from the former condition.

Pathological examination of the eye removed from Case 3. Fixation was by Bouin's fluid. After removal from this the eye was washed with water, and in doing so a rough patch was observed near the posterior pole and scrapings from this showed numerous small crystals lying for the most part along the remains of a blood vessel. Unfortunately the specimen was mounted in balsam in the expectation that other scrapings would shew the same, and could be used for a micro-chemical test. This was not however the case, and no other scrapings gave any uric acid reaction when treated with Benedict's uric acid reagent by a friend doing biochemistry. The fact that no other area showed crystals, plus the fact that similar crystals were found in a neighbouring area in some sections seems to negative the possibility that they were artefacts.

In order not to disturb the lens, the eye was cut in half by a coronal incision. In doing so the vitreous was found to be very unusually tough. The anterior half remained in position, the posterior fell out. This latter part was sectioned at once, and tested for uric acid but gave no reaction. It was composed of fine fibrils of collagenous material containing practically no cells. It was evident however that very little actual vitreous was left, or its substance had been completely pervaded by collagenous material which had formed fine fibrillae.

The examination of the rest of the eye was made after embedding in celloidin, and various changes were found which were in accord with the clinical observations.

The cornea was of somewhat loose texture at its margins, but there was no cell infiltration. The abnormality may have been an artefract. Although the aqueous had been clear clinically it had contained much albuminous material, as almost the whole of the anterior chamber was filled with the same fine coagulum as had been seen in the vitreous. It was most dense near the cornea, and shrinkage here had produced a line of rounded spaces next to the endothelium. No cells were present anywhere, in contrast to what is found in ordinary recurrent iritis.

On the outer surface of the globe, from where the conjunctiva begins, there was a great thickening of the sclerotic which was as nearly as may be double its normal measurement. Part of this

is due to an episcleral change, the tissue being full of new blood vessels and cells. This is seen in the photograph Fig. 1.

Deeper than this there is also much vascularity, but the more superficial parts of the sclera proper are full of lymphocytes and plasma cells. There are also numerous spaces between the fibres which contain new collagenous material in fine fibrillae.

Fig. 2 shows the external half of the sclerotic, while Fig. 3 is of the internal portion.

In this latter the changes are even greater. The scleral fibres are spaced out by collagenous exudate, staining with eosin or acid fuchsin, and shewing fine fibrillae. There is however no necrotic change anywhere such as one sees in tuberculous disease. As one passes towards the choroid the quantity of plasma cells and lymphocytes increases so that the normal boundaries of sclera and choroid are lost, save for traces of the lamina supra-choroidea, and the choroid in front is represented only by scattered pigment. The retina begins with a much swollen ora serrata, passing into cystic spaces, and further back is detached, the subretinal space being filled with fine fibrillary exudate with large oval cells.

The ciliary body is increased in size as a result of the separation of its fibres by fibrillary exudate, with clumps of lymphocytes, and in all sections of the iris a large collection of lymphocytes is present near the root.

All through the iris may be seen inflammatory cells, but not in numbers correponding to the very numerous attacks of inflammation. This discrepancy is most marked near the tip of the iris, where the arterioles and venules pass into each other, and where in consequence there is to be found in cases of iritis a large number of cells. In this case they are absent (Fig. 4).

There seems to be no destruction of uveal tissue, and hardly any evidence of its adhesion to the lens capsule. This agrees with the scanty synechiae which were seen *intra vitam*.

The whole space round about the lens is full of the same fine fibrillary coagulum seen in the aqueous and vitreous.

The retina shews signs of oedema in the loss of regularity of the layers, but there is no cellular invasion or destruction till one reaches the membrana limitans externa.

Beyond this however there is a striking change in the complete destruction of the bacillary layer, except over that part of the nasal periphery, which accounts for the loss of light perception except far out in the temporal field (Figs. 5 and 6).

Immediately outside the membrana externa is a line of débris which hardly stains. This, with contraction spaces, is all that is left of the rods and cones. The hexagonal pigment is somewhat lacking in its acicular pigment, as judged by the ease with which

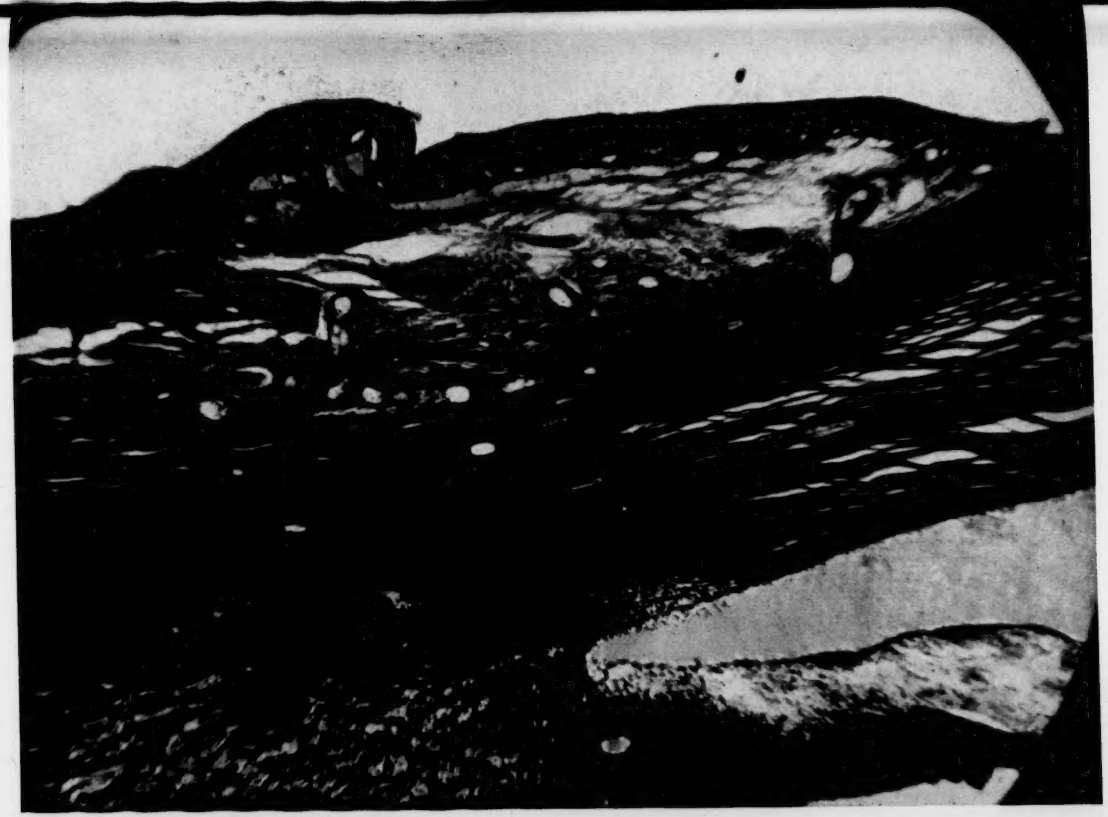


FIG. 1.

The corneo-sclerotic junction. Shows the thickening of the episcleral tissues with enlarged blood vessels. There are lymphocyte masses in the ciliary body, and at the root of the iris. The fibres of the ciliary body are spaced out by collagenous exudate showing under a high power fine fibrillary structure. The anterior chamber is full of a fine coagulum.

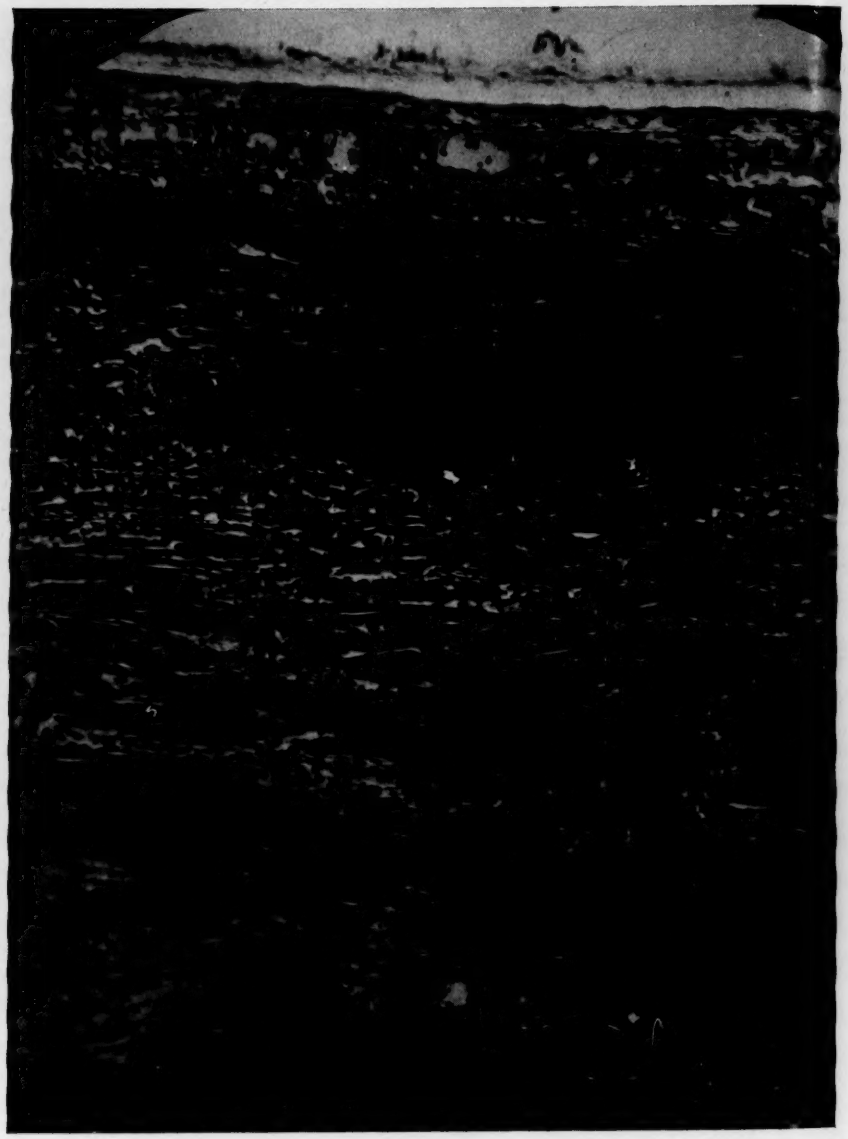


FIG. 2.

The outer part of the sclerotic just behind the ciliary body. Its great thickening is due to separation of the fibres by cells and collagenous material. A clump of lymphocytes can be seen.

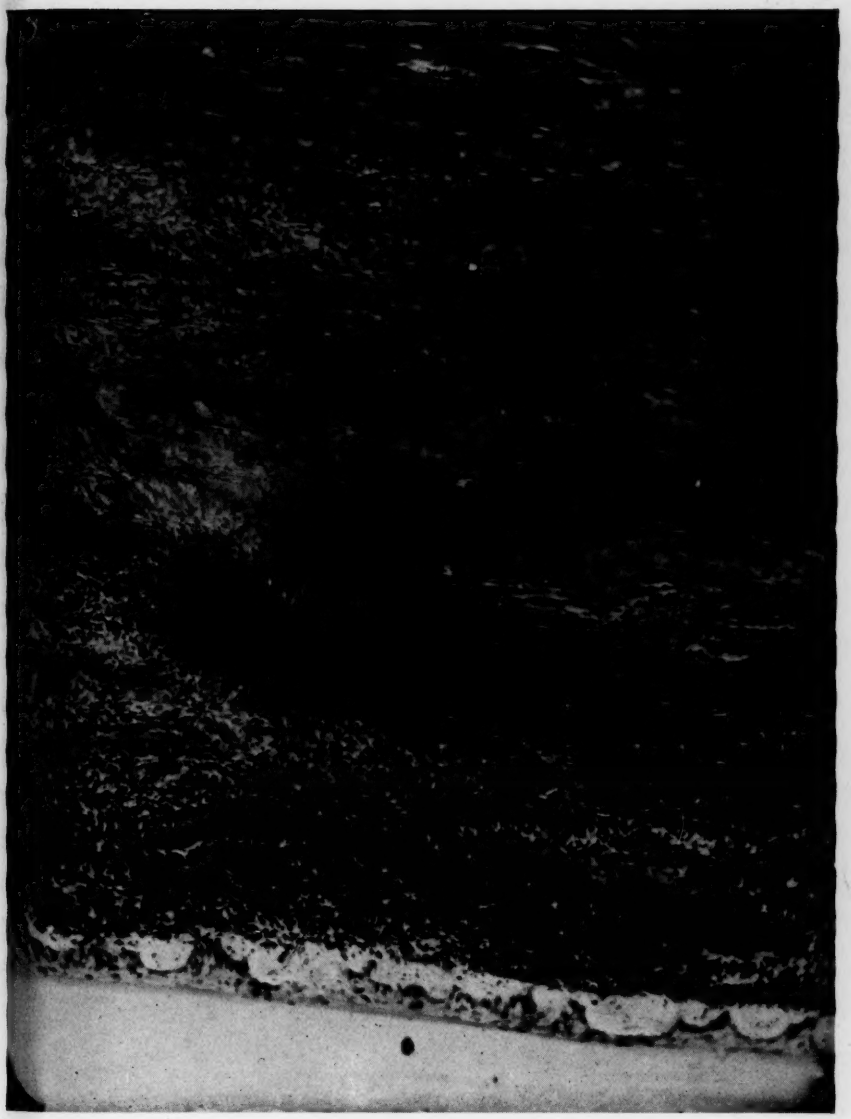


FIG. 3.

The deepest part of the sclerotic from the same region. There is more collagenous exudate, with cells and scattered pigment granules. The lamina suprachoroidea cannot be made out. The deepest part represents the anterior part of the choroid, it is full of cells but hardly any blood vessels are visible.

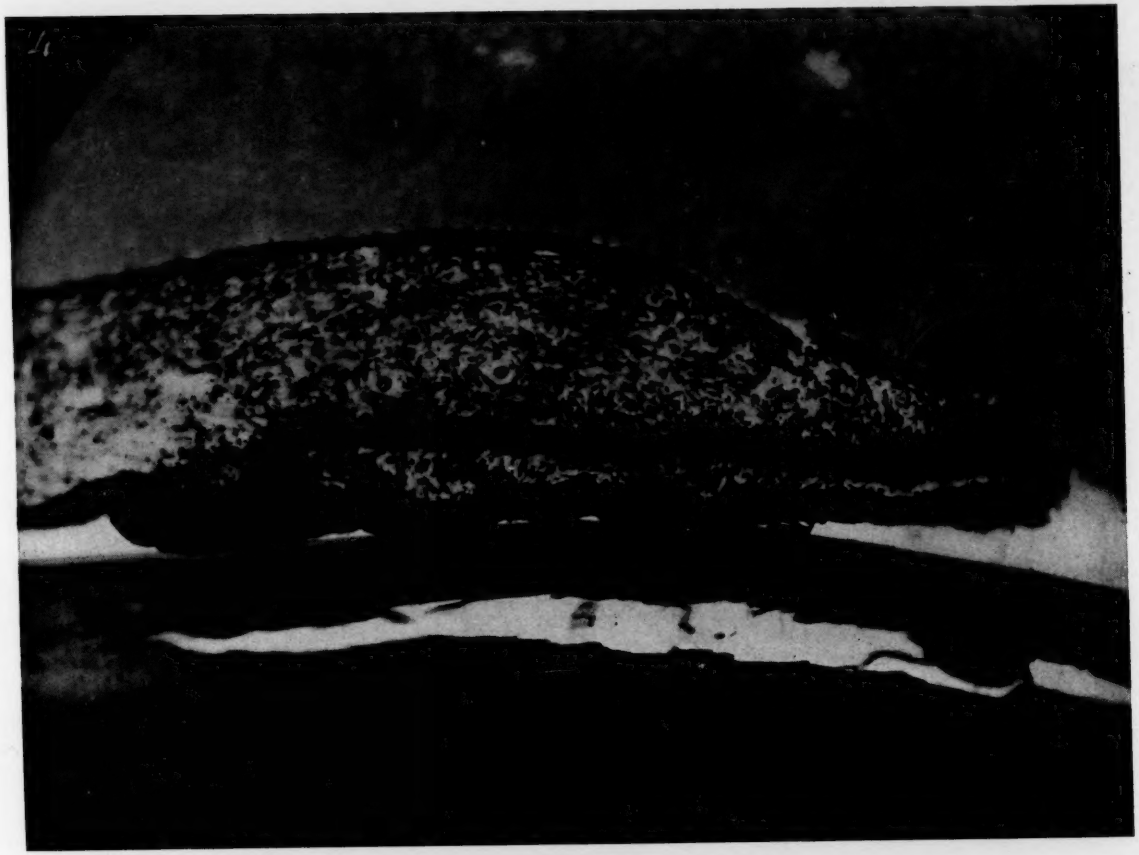


FIG. 4.

Tip of iris. Despite the scores of attacks of iritis there is comparatively little damage. There is no collection of lymphocytes in the area of transition between arteries and veins near the pupillary margin. Sphincter is normal. Uvea unaltered.

There is no collection of lymphocytes in the area of transition between arteries and veins near the pupillary margin. Sphincter is normal. Uvea unaltered.

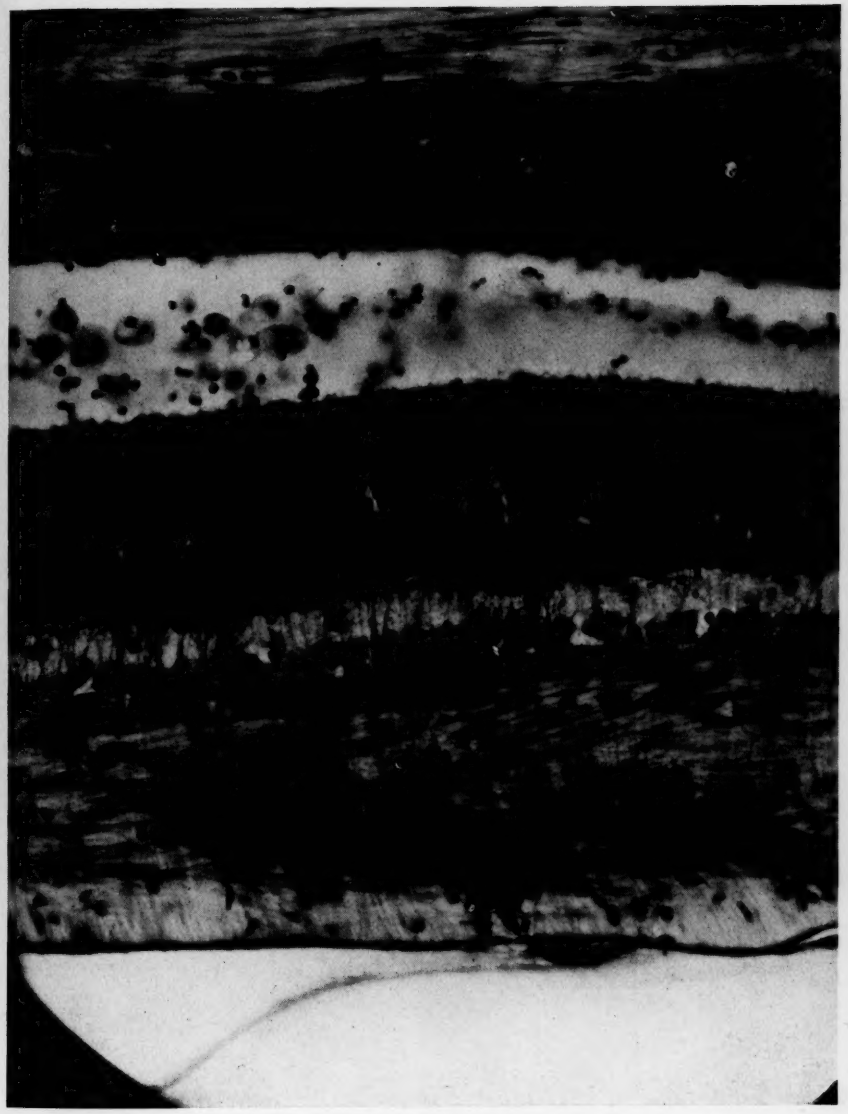


FIG. 5.

Choroid and retina. The former is avascular, but contains many cells mainly lymphocytes. The subretinal space is full of coagulum with large oval cells, containing pigment. There is no trace of the bacillary layer save an irregular non-staining line.

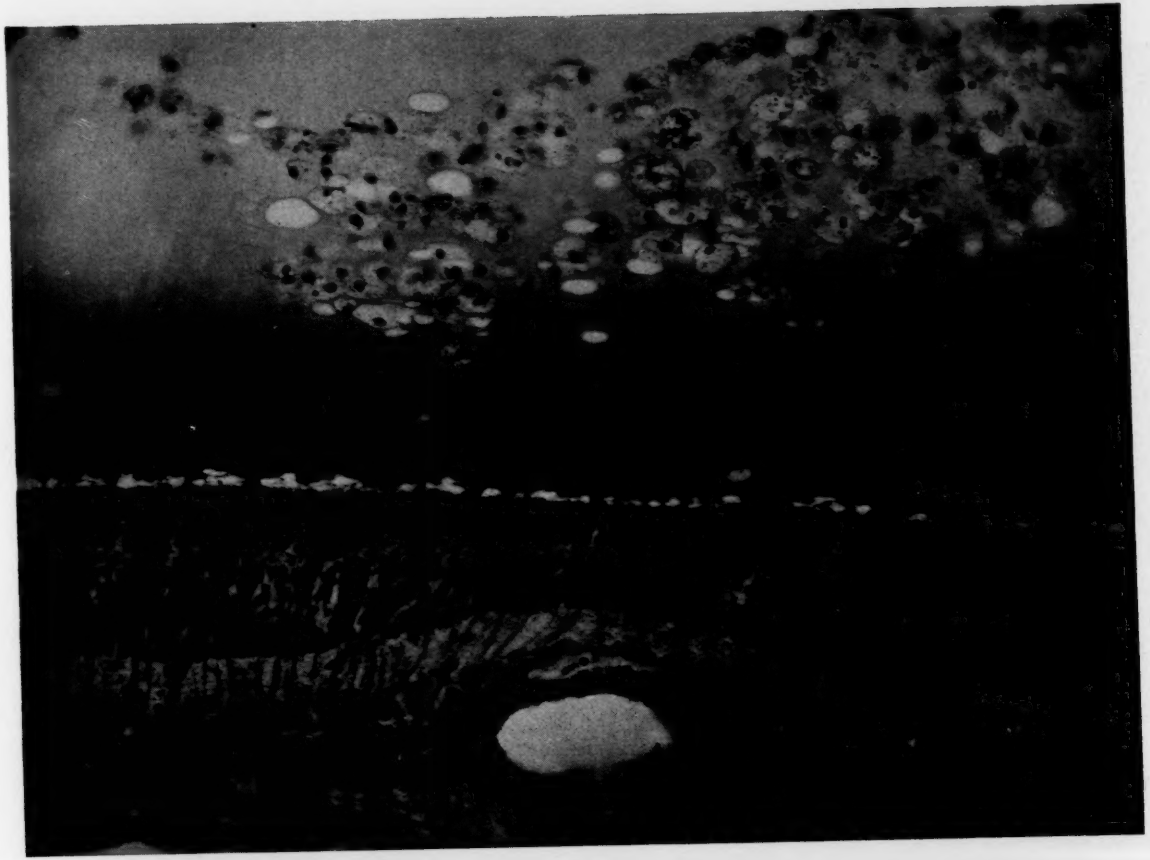


FIG. 6.

The large cells from the subretinal space. The clear rounded spaces next the membrana externa are produced by fixation contraction.

next the membrana externa are produced by fixation contraction.

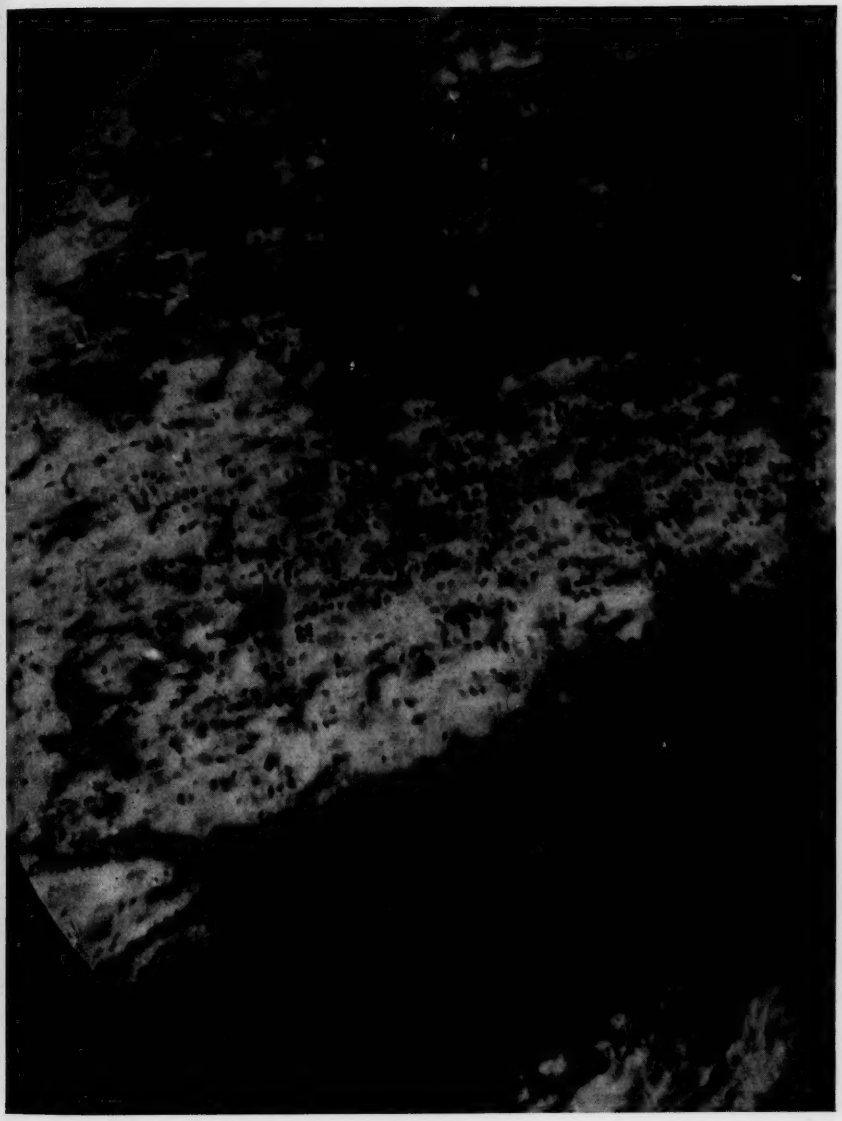


FIG. 7.

Crystals on and in Tenon's capsule near the optic nerve. The dark objects and clear rings are haemocytes. (×480.)

its nuclei are seen. In the coagulum in front are numbers of large oval cells which contain pigment of the acicular type. These cells are from ten to as much a forty μ in their longest diameter, and possess a small irregular nucleus. Their outline is very clear and sharp as indicated in the photographs. I suggested in the July, 1935, issue of this Journal that one of the functions of the membrana limitans externa was to form, with the lamina vitrea, a lymph space for the nutrition of the rods and cones lying in it. In this case these have been destroyed, while outside the retina is scarcely altered. The suggestion of some irritant in the lymph seems natural, even allowing for the fact that the rods and cones are easily damaged.

The choroid is avascular and full of cells. One cannot make out any chorio-capillaris. In the anterior part are lymphocyte collections but nowhere large. The optic nerve appears to be free from inflammatory change.

On the posterior surface of the sclerotic there are, at one or two spots, myriads of tiny brown crystals. The brown tint is seen with a magnification of about 100, but the individual crystals need a twelfth inch. They are about the size of average bacteria, but as they lie in different planes I have failed to get a sharp photograph of them. Fig. 7 gives an idea of their numbers and of their size compared with haemocytes. Again it was unlucky that the crystals were found in a mounted specimen so that chemical tests were not possible. The patient had had many attacks of what were in part Tenonitis, and it is not unreasonable to conclude that these crystals, and those seen once in the cornea, were urates.

It would seem that there has been a definite selective action by the tissue irritant, as the sclerotic, the choroid, and the bacillary layer of the retina have been seriously damaged, while the iris and to a less extent the ciliary body have escaped. The lens remained clear.

The proof that gout is the principal cause is partly negative, in that the pathological conditions do not resemble any others which I have seen. On the positive side are to be placed the fact that in 3 cases Tenonitis was present, and that episcleritis periodica fugax was the commencement in all the cases. In three cases the patient's diet and use of alcohol were such as would naturally produce a gouty condition, and in one the cessation of beer, and diminution of heavy meat diet put an end to the troubles. Besides these points we found that in the two where an examination was made the uric acid content in the blood was greatly increased during the acute attacks.

THE SWELLING PRESSURES OF NORMAL AND GLAUCOMATOUS VITREOUS BODIES

BY

SIR STEWART DUKE-ELDER, HUGH DAVSON
and GRAHAM HARVEY BENHAM

FROM THE DEPARTMENT OF PHYSIOLOGY AND BIOCHEMISTRY,
UNIVERSITY COLLEGE, LONDON

IN earlier studies (Duke-Elder *et al.*, 1935; Duke-Elder and Davson, 1935) the possibility was discussed that a swelling of the vitreous body is the cause of primary chronic glaucoma. The results obtained pointed against the theory, but till now a decisive proof has been lacking. In the present work a technique for measuring the swelling pressure of the vitreous body has been developed and applied to normal and glaucomatous vitreous bodies. If a swelling of the vitreous body is responsible for the raised intra-ocular pressure in primary chronic glaucoma, then it would seem to be necessary that its swelling pressure in this disease must be greater than normal. The present investigation was undertaken primarily with a view to settle this point.

The observation by Duke-Elder (1930) that the isolated vitreous proteins only swell to about forty times their weight in water, in conjunction with certain other facts led us to believe that the vitreous body has been formed as a clot from a sol (Duke-Elder and Davson, 1935) so that dehydration by pressure was considered as an essentially irreversible phenomenon producing states of instability; it was thus considered as incorrect to speak of a true swelling pressure in this case. Baurmann (1934), however, has shown that if the vitreous proteins are not allowed to dry during their preparation they may be made to swell back to a dilution of the same order as that in the original vitreous body from which they were derived. It thus seems that the vitreous body is formed by a process of swelling and not as a dilute clot from a sol and that a genuine swelling pressure ***must exist however small*** at all states removed from the swelling maximum.

In considering the rôle of the swelling pressure of the vitreous body in glaucoma from the theoretical point of view, it would not be necessary for the abnormal swelling pressure of the gel to be equal to the difference in pressure between the normal and the glaucomatous eye. The exact amount of the increase which would be necessary is difficult to determine for any individual case, as it might depend on the vascular changes accompanying the raised intra-ocular pressure. Thus if the vitreous body were to exhibit a

very slightly raised swelling pressure it would absorb water and swell, thereby increasing the intra-ocular pressure. However, the capillary pressure would of necessity rise in response to the raised intra-ocular pressure in a purely mechanical way (Duke-Elder, 1926), so that the condition ***intra-ocular pressure=capillary pressure—Donnan osmotic difference*** would be satisfied and equilibrium would be established at a new level. The vitreous body would therefore be able to attract more water, and as the rise in intra-ocular pressure produced in this way would also be accompanied by a rise in the vascular pressures, one can conceive a gradual mounting up of the pressure far greater than the swelling pressure of the vitreous body in its postulated abnormal state. The problem therefore resolves itself into placing a lower limit on the swelling pressure required to produce a final state of tension of (say) 60 mm. Hg. If the swelling of the vitreous body is to cause a raised intra-ocular pressure, the extra water held by it must come from the capillaries, since only in this way will the total volume of the eye-contents be increased; although if the force with which the vitreous body attracts this water is very small, *i.e.*, if the swelling pressure is very small, the vitreous body will satisfy its demands for water at the expense of the fluid in the eye rather than from the capillaries since in the former case no work against an external pressure will have to be done. It is well known that in a number of cases of absolute glaucoma fluid in considerable quantities is found in the vitreous cavity; in fact this excess of fluid seems to push forward the lens, diminish the anterior chamber, compress the ciliary body, choroid and retina, and to be the ultimate cause of the raised pressure of the eye. If this accumulation of fluid and its retention is due to its being held by the vitreous gel owing to an increase of its swelling pressure, then, in view of the theoretical arguments put forward in this paragraph, we may say *for the purposes of argument*, that the swelling pressure of the vitreous body in glaucoma of this type must be *at least* of the order of 1 mm. Hg. If it can be shown to be greater than this, the theory that an abnormally increased swelling pressure in the gel is responsible for primary chronic glaucoma receives more support. If it is shown that the swelling pressure is less than this, then it would appear to be advisable to seek in some other physico-chemical mechanism an explanation of the pathological phenomena we are investigating. If, on the other hand, there appears to be no difference in swelling pressure between the normal and abnormal vitreous gel, and especially if both values are small, the hypothesis must be rejected.

The results of the measurements described in this paper show that the swelling pressure of a glaucomatous human vitreous body is not sufficient to account for the raised tension.

Experimental

The principle of the apparatus is illustrated in Fig. 1. Chamber A contains a sintered glass plate, B, and is connected to a graduated tube C by rubber tubing. The apparatus is filled with Ringer solution and by manipulation of T_1 and C the latter is adjusted so that the fluid just wets the plate B while the meniscus and the plate are on the same level. The vitreous body is placed in A after

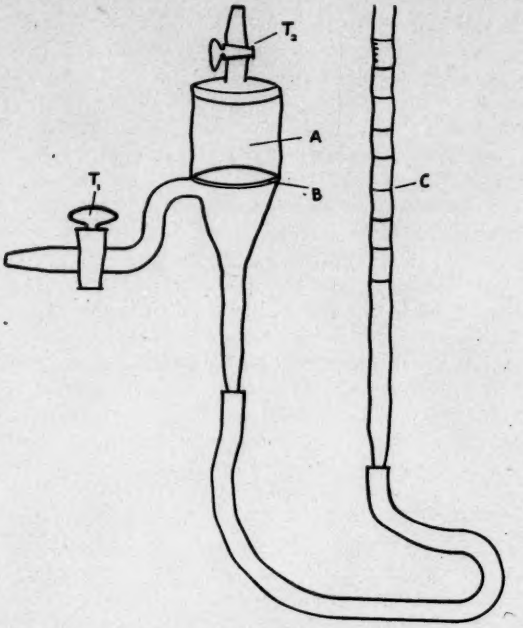


FIG. 1.

closing T_1 and C is raised so that the meniscus in C is at the same level as the top of the vitreous body. T_2 is kept open during the whole of the experiment. By lowering C any required pressure may be exerted on the vitreous body, so that water is withdrawn from it. The meniscus rises into C until the difference in level between the meniscus in C and the top of the vitreous body in A represents the swelling pressure of the vitreous body at the given state of dehydration. Thus if the tube is lowered by 2 cm. and the meniscus rises so that the difference in level is 1 mm., the swelling pressure may be said to be not greater than 1 mm. saline over the volume change corresponding to the loss of water produced in

this way. The volume change is measured by observing the changes in height of the meniscus in the graduated tube and multiplying by the cross-sectional area. To obtain an exact value of the swelling pressure would take a long time as a film of protein is formed on the porous plate through which water filters only very slowly; however, as the purpose of these experiments is to investigate whether a swelling pressure of at least 1 or 2 mm. Hg exists, it is sufficient to note the position of the meniscus after a short time and regard the pressure registered as an upper limit.

Normal, dialysed and KCNS-treated ox vitreous bodies and a human glaucomatous vitreous body were used; in the last case the vitreous body was taken from a freshly enucleated eye in absolute glaucoma with high tension.*

Results

With all the vitreous bodies examined identical results were obtained; the upper limit of the swelling pressure at volumes of 100 to <1 being within the experimental error (1-2 mm. saline). To illustrate the method the protocol from a normal vitreous body is shown.

Volume of vitreous body	Time	Swelling pressure
100—59 ...	1 hour ...	>7 mm. saline
59—57 ...	2 hours ...	>4 „ „
57—56 ...	3 „ ...	>2 „ „
56—16 ...	24 „ ...	>1 „ „
16—<1 ...	30 „ ...	>3 „ „

From this protocol it is seen that at the volumes 56 to 16 the pressure was >1-2 mm. saline (the limits of experimental errors); from this it may be inferred that at all volumes greater than 16 the swelling pressure must be less than this value, since the swelling pressure of a gel decreases with increasing volume. This was confirmed in other experiments in which attention was concentrated on the earlier phases of dehydration in so far as it was shown that the swelling pressures here also fell within the limits of experimental error. From the same protocol it appears that at a volume of <1 the swelling pressure is >3 mm. saline; from other experiments where attention was concentrated on this phase the limit could be brought down to 1-2 mm. saline as with greater volumes. By a volume of <1 is meant the volume of the vitreous body when it appears as a hydrated skin on the porous plate with a volume of perhaps 0·05 ml. In this region the volume of gel

*We are indebted to Dr. Briggs, of Moorfields Hospital, for providing us with this eye

remaining is too small to allow of the measurement of any further changes in hydration with pressure with the experimental arrangement used, so that all experiments had to stop when this state was reached. As will be shown in this discussion, it is probable that the swelling pressure reaches considerable magnitudes in this region. However the aim of the experiments described here are primarily to determine the swelling pressures at volumes only slightly removed from normal as, in the case of a glaucomatous vitreous body, it is the pressure in this region which determines the possibility of its swelling *in vivo* against an externally imposed force.

Discussion

The first conclusion to be drawn from the results is that the ***swelling pressure of the vitreous body cannot be an aetiological factor in primary glaucoma.*** The most surprising feature of the results is the failure of the vitreous body to exhibit a swelling pressure of 1-2 mm. saline or more even when dehydrated by over 99 per cent.; further, it might at first sight have been expected that a strong hydrating agent like KCNS would have produced a swelling pressure of this order or greater in this range of volumes, but such was not the case; the result is in general agreement with earlier findings on the elasticity (Duke-Elder and Davson, 1935). The results allow of some interesting conclusions in regard to the nature of the vitreous body. Thus, in the first place, since the vitreous body has very pronounced elastic properties and contains only 0·025 per cent. of the gel-forming protein (Duke-Elder, 1930), it must be concluded that the protein micelles are linked together in branching chains, a conclusion already suggested by another physico-chemical line of approach (Duke-Elder and Robinson, 1934). With a gel of such low protein content there can be no possibility that the bulk of water is held by hydration forces, *i.e.*, electrostatic attraction of water dipoles, as the following considerations will show. From the titration curve of the vitreous protein (Duke-Elder, 1930), it appears that at normal pH about 60×10^{-5} equivalents of base are bound by one gramme of protein. With a normal vitreous body this would mean $1{\cdot}5 \times 10^{-7}$ equivalents per ml. and roughly corresponds to the number of $-COO^-$ ions per ml. of vitreous body. Assuming for simplicity that they are distributed in a cubic lattice, their distance apart, l, will be given by substitution in the formula:

$$l = \sqrt{\frac{1}{NC}}$$

where N is Avogradro's number and C the concentration of $-COO^-$ ions in equivalents per ml. By substitution in this way a value for l equal to 2×10^{-6} cm. or 200 Ångström units is obtained.

Born (1927) has shown that the radius of the Li + ion plus its hydration sheath is 2·26Å, whilst the radius of the ion itself is 0·45Å; the forces of hydration, in this case operate over a distance 1·81Å, As the Li + ion is far more heavily hydrated than the $-COO^-$ ion, and further, as Hartley (1936) has pointed out, as there is no reason to suppose that the $-COO^-$ in a protein micelle

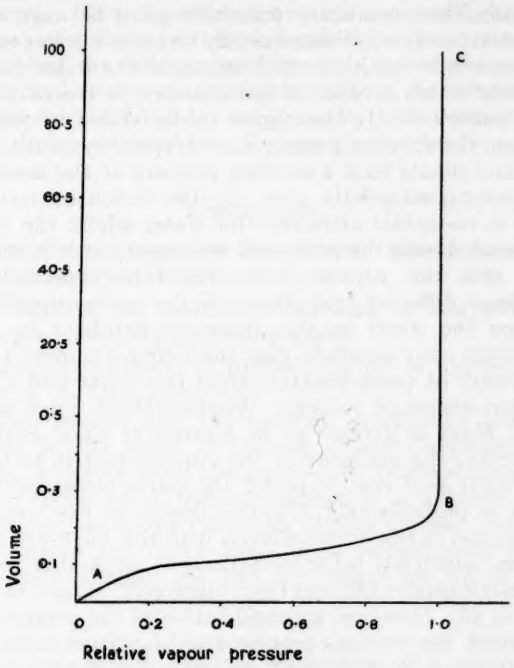


FIG. 2.

will have a very different hydration from that of the $-COO^-$ ion in Na acetate, it is evident that it is quite out of the question to consider the existence of any pull on the water molecules at distances of 100Å.

These considerations are confirmed by the vapour pressure isotherm of the vitreous body. In Fig 2 a curve showing the vapour pressures of the vitreous body at different water contents is shown. The figures used for plotting this curve are taken from Duke-Elder (1930) and are corrected approximately for the salt content of the vitreous body. In order to bring out the typical S-shape of the curve at low volumes, the ordinates above a volume

of 0·5 ml. are one hundred times those below this value. Thus if the curve were drawn with the ordinates equal all the way up the vertical distance between B and C would be approximately one hundred times that between B and A. The vapour pressure of the vitreous body only begins to decrease at a volume of 0·3 per cent. of the original volume, so that it is at this point that any appreciable diminution of the activity of the water molecules occurs. At the point B, then, there is a sharp transition point between water held by electrostatic and co-ordinate valency forces and water not so held.

Thus there is a duality in the nature of the water held by the vitreous body which is reflected in its numerous macro- and microscopical peculiarities. In this region characterized by the part AB of the graph the vitreous protein has a typical lyophilic attraction for water and should have a swelling pressure of the same order as that of concentrated gelatin gels. In the region characterized by BC there is no actual attraction for water whilst the amount of water associated with the protein is very great; it is in this region, therefore, that the vitreous body would be expected to show characteristics different from those of the conventionally studied gels. Since the water in this region is not held by hydration forces, one can only conclude that the vitreous protein is oriented in a framework of pores which contain this water and so give the gel a certain degree of solidity. Whether these pores are formed by parallel fibres of protein or by a series of spiral chains is not easy to decide; the similarity of the vitreous protein to the scleroproteins might lead one to prefer the latter possibility (Astbury, 1933). It is probable that it is this duality in the nature of the water contained in the vitreous body, with the huge preponderance of one form, which has led some authors to think that the vitreous body is fundamentally different from other gels, in fact, to deny that it is a gel at all. However, a consideration of the parallel processes of swelling of the vitreous protein and of gelatin (say) in water, shows that the difference is by no means so fundamental as to preclude the vitreous body from the category of gels. Thus when the former swells there is an initial strong hydration of the protein micelles whereby the chains are separated and oriented to form pores. The hydration, by inducing ionisation of the —COOH groups, produces net negative charges at localised points in the chains; these negative charges repel each other, thus enlarging the pores and making room for more and more water. With gelatin the same process of hydration and pore formation occurs but the forces of hydration are strong enough to rupture the micellar linkages before the pores expand to anything like the extent they do in the vitreous body, so that the gel passes into a sol. Thus the essential difference between the gel-forming powers of gelatin and the vitreous protein resides in the power of the micellar units of

the latter to adhere to each other and resist the hydration forces which tend to rupture them.

It may be objected that in explaining the nature in which the water is associated with the vitreous body we have rejected the idea that an electrostatic attraction for water dipoles may occur over large ranges, whilst retaining the notion that an electrostatic repulsion between two negative charges may operate over comparable distances. This objection is by no means valid, however, as the attraction of a central ion for a dipole depends on a number of factors including the divergence of the field round the central ion and the thermal energy of the dipole, so that the effectiveness of the attractive force falls off far more rapidly with distance than in the case of the repulsion of two like non-dipolar charges.

Conclusions

1. The swelling pressure of the normal vitreous body is very small—less than 1 to 2 mm. saline.

2. This value is not materially increased by dialysation or in the presence of a strong hydrating agent.

3. The swelling pressure of the vitreous gel in chronic primary glaucoma is of the same order.

It therefore follows that the swelling pressure of the vitreous body cannot be the cause of chronic primary glaucoma. It is proposed in a forthcoming publication to produce experimental evidence in favour of a theory implicating a different physico-chemical mechanism in the causation of this disease. Some theoretical deductions are made from these experiments as to the structure of the vitreous gel and the means by which it holds its water.

We gratefully acknowledge our indebtedness to Professor Freundlich and Mr. Hartley, of the Chemistry Department, for advice and criticism and to the Medical Research Council for personal grants to two of us (H. D. and G. H. B.) and for defraying the whole expenses of this work.

REFERENCES

Astbury.—Fundamentals of fibre structure. London, 1933.

Baurmann.—*Arch. f. Ophthal.*, Vol. CXXXII, p. 302, 1934.

Born.—*Z. Electrochem.*, Vol. XXVI, p. 401, 1927.

Duke-Elder.—*Jl. of Physiol.*, Vol. LXI, p. 409, 1926; *Brit. Jl. of Ophthal.*, Vol. X, p. 513, 1926.

——— *Brit. Jl. of Ophthal.*, Monograph, Supplement IV, 1930.

Duke-Elder and Davson.—*Biochem. Jl.*, Vol. XXIV, p. 1121, 1935: *Brit. Jl. of Ophthal.*, Vol. XIX, p. 433, 1935.

Duke-Elder and Robertson.—*Brit. Jl. of Ophthal.*, Vol. XVIII, p. 433, 1934.

Duke-Elder, Davson and Robertson.—*Biochem. Jl.*, Vol. XXIX, p. 72, 1935.

Hartley.—Aqueous solutions of paraffin chain salts, p. 59. Paris, 1936.

GLYCEROL TRINITRATE (nitroglycerine) IN THE TREATMENT OF HEMERALOPIA (night-blindness)

BY

R. DE R. BARONDES, M.D.

SAN FRANCISCO

HEMEROLOPIA, often miscalled nyctalopia, is characterised by a difficulty in adapting or an inability to adapt the faculty of vision to faint illumination. Some of the causes ascribed to this condition are:[1]

The influence of direct light of the sun during daylight, exposure, and overwork,
Nutritional deficiency (vitamin A),
Intra-ocular diseases, etc., as retinitis pigmentosa, optic atrophy, glaucoma, choroiditis. (*Also included here should be mentioned arteriosclerosis, miosis, syphilis, and toxicosis such as excessive use of tobacco, coffee, and vaso-constricting drugs.*)
Brain disorders,
Idiopathic and hereditary influences.

To these causes of hemeralopia should be added one other, namely, a circulatory disturbance, or dysfunction, in which the retinal arteries and capillaries remain in a spastic state. This spasticity is observed to be more pronounced in those vessels in the fringe of the retina, that part of the retina having to do with vision under faint illumination. The nerve-endings in this light-perceiving area—the retinal rods—are dependent upon a proper supply of food for the regeneration of visual purple, the "night seeing agent."

As is known, visual purple is a very light sensitive substance of a rose colour, which the rods of the deepest layer of the retina are tipped with. Under normal and ordinary circumstances of bright light, visual purple bleaches to yellow, splitting off carotene during the process, and is constantly being regenerated when the eye is at rest in the dark. Visual purple is stored in the posterior portion of the cells of the pigment epithelium, and after light exposure, the pigment granules push their way inward into the processes that extend between the rods and cones, and the latter contract and shorten. These terminal organs of the optic nerve receive the waves of light falling upon the retina, converting these vibrations into impulses which are carried by the optic nerves and tracts to the brain where they produce the sensation of light[2].

When the retinal arteries, arterioles and capillaries become

spastic, or mildly sclerosed, as a result of disturbances of innervation, etc., these vessels are unable to carry or deliver the proper amount of blood to the nerve-endings in the light-perceiving layer of the retina. There then results a state of nutritional insufficiency to these parts and a metabolic increase of the visual purple cannot take place. Without ample regeneration, a depletion of this night-seeing agent results in a consequent poor reaction to faint illumination.

Exposure to light causes a disturbance in the metabolism of the visual purple; the more prolonged the exposure to bright light, the more rapid a depletion of this pigment. In some manner not as yet clearly understood, the retinal rods cells synthesize, utilise or " absorb " vitamin A (and perhaps the metabolic stimulant, vitamin B). Vitamin A is the important factor in the regeneration of this visual purple. If sufficient vitamin A is not " absorbed " by the retinal rod cells as a result of circulatory disturbance, ample regenerations of visual purple cannot take place.

It is known that very small amounts of vitamin A in the diet will relieve certain cases of functional night-blindness[4]. There have been many cases though of night-blindness developing in individuals whose diet contained an abundance of it. Dr. Y. Fujihira[3] reported many cases of night-blindness in two Japanese regiments. Examination of the food given these soldiers convinced the medical officer that the direct cause of this disease was not the lack of vitamin A, but the influence of the sun during the day-time drill, and overwork.

Though the daily intake of a well-balanced diet may be adequate for the body's general needs, an insufficiency may still exist; and care should be exercised in ascribing certain diseases to nutritional deficiences when the causative factor is one of true circulatory insufficiency. As Wilbur and Eusterman state: " It is worthy of emphasis, that states of nutritional deficiency may arise, as in this case, not as a result of inadequate intake of vitamins or other foodstuff but as a result of gastro-intestinal or other disturbances " (*circulatory-nutrition deficiency*) " interfering with either the normal digestion and assimilation of foodstuff or their metabolic activity[1]."

Hemeralopes may see normally during daylight while in bright illumination, but on approach of twilight, or on entering dimly illuminated places, have considerable difficulty in orienting themselves to this faint illumination. On suddenly coming from bright sunlight into semi-darkness, objects and dim-lights appear to take on a yellow-amber hue, and on leaving darkness to enter sunlight, cases complain of photophobia. These individuals have constricted visual fields and have considerable difficulty in seeing objects on one side while looking straight ahead. This is because the area of the

rods in the retina not only serves for the night-vision but also is the means by which objects are seen out of the direct line of vision. It is this peripheral vision that enables one to become instantly conscious of moving traffic on one side or the other.

Ophthalmoscopic findings on five adult cases of hemeralopia proved most interesting. These cases presented a constricted blanched appearance of the peripheral portions of the retinal arteries, and with more or less venous hyperaemia and congestion. Experiments were carried on with various vaso-dilating drugs to note their action on these spastic retinal vessels. Nitroglycerine proved to be the most effective dilator of these although the nitrites —amyl, sodium, etc.—gave almost comparable results. It was observed that after the adminstration of nitroglycerine (0·003—0·06 gm.), for the first few minutes, the eyes' sensitivity to faint objects seen from the side was less than normal. However, from five to ten minutes later, the eyes' sensitivity to faint light was markedly increased, the patients having no difficulty in moving about the darkened room. In two of the subjects, the olfactory sense, and the gustatory sense became more acute. No changes were observed in the sense of hearing, but there was a complaint at first of poor equilibrium, vertigo, throbbing in the head, etc. After the first few doses though, these symptoms were no longer complained of.

Nitroglycerine is more or less volatile, and if exposed to air loses much of its strength. Coated tablets were used in these studies, insuring proper and accurate dosage. Care should be used in its administration, because of its effect on the central nervous system, blood pressure, etc.

It is important to note that, if actual degenerative changes have taken place in the walls of the arteries, such as may be found in cases of advanced arteriosclerosis where the muscle fibres have been replaced by connective tissue, etc., nitroglycerine would be incapable of dilating such vessels, and, a night-blindness the result of such a condition would not be benefited by this or any other form of therapy.

It is suggested that proper doses of the vaso-dilator drugs might be administered to those working more or less continuously in the dark and to whom it is especially important to be able to see in darkness, such as spies in wartime, navigators and aviators who do night-flying[5].

Curiously enough, no comprehensive study of hemeralopia and its treatment has appeared in the literature. It is odd that this fairly common condition is overlooked in the study of the eye, and its detection in an ordinary routine examination. No doubt there are many who suffer from night-blindness but are not aware of it.

A routine examination for night-blindness probably would reveal many more cases than are now suspected[4].

Since case records indicate that nitroglycerine and other vasodilators gave excellent results in the treatment of this condition, and, since untoward effects were absent, further trials with this method seem justified[5].

BIBLIOGRAPHY

1. **Wilbur, Dwight and Eusterman, G. B.**—Nutritional night-blindness. *Jl. Amer. Med. Assoc.*, Vol. CII, pp. 364-366, February 3, 1934.
2. **May's** Manual of the Diseases of the Eye.
3. **Dr. Med. Yozoh Fujihira.**—Die ätiologische Betrachtung uber die spontane Nachtblindheit bei den Japanischen Soldaten. Band XII, Heft 6, Juni, 1934, Sonderabdruck aus dem Chiba Igakki, Zasshi.
4. **Jeans, P. C. and Zentmire, Z.**—A clinical method for determining moderate degrees of vitamin A deficiency. *Jl. Amer. Med. Assoc.*, Vol. CII, 12, p. 892, March 24, 1934.
5. I am indebted to Dr. H. Alexander Brown, M.D., F.A.C.S., San Francisco, for his helpful co-operation and assistance in these tests; and to Drs. P. Lazoreve and L. Teile, Leningrad, for their articles on similar research.

CATARACTA BRUNESCENS—STUDY OF THE NATURE OF THE COLOURING SUBSTANCE

BY

PROFESSOR DR. ELENA PUȘCARIU *and*

DR. JULIUS NITZULESCU

FROM THE OPHTHALMOLOGICAL CLINICS AT JASSY, ROUMANIA
DIRECTOR: PROFESSOR DR. ELENA PUSCARIU

Clinical Considerations

CATARACTA Nigra (Wentzel, 1788) or more correctly named Cataracta Brunescens (Becker, 1881), because in the large majority of cases the lens presents only a more or less deep brown colour, is a rather unusual form of cataract. In our practice we have met it only four times among a total of 1,357 cases of cataract.

Some authors believe that it appears especially in myopic eyes, but only one of our four cases was short-sighted. Jess, Rollet Bussy considered that cataracta brunescens has a definitely worse prognosis than an ordinary cataract. They have frequently observed the appearance of iridocyclitis or of infections after the operation, perhaps due to the special predispositon produced by the high myopia. Our cases, just as those of Gifford and others, did not confirm this unfavourable prognosis. All four had a perfectly normal post-operative course.

Our observations can be summarised as follows:—*Case* 1. A peasant, aged 56 years, entered the clinic on October 19, 1925. The impairment of sight began a year previously in the left eye,

and six months later in the right. There had been no pain or inflammatory phenomena. On admission R.V.=counts fingers at 1 m. L.V. counts fingers at 0·60 cms. Skiascopic examination, which was possible in the R.E. only, showed a myopia of 7 D. The posterior polar cataract permitted the examination of the fundus, showing peripapillary choroidal atrophy. Intra-ocular pressure in both eyes 18 mm. Blood Wassermann negative. The left eye was operated on November 6, 1925. Extraction with iridectomy and capsulectomy. The lens was deep brown. Post-operative course normal. The sight remained, however, weak due to the numerous foci of choroidal atrophy.

Case 2. S. R., aged 62 years. Admitted June 28, 1932. The sight began to diminish in 1916. In 1918 she had her left eye operated on in another hospital. At the present time R.V. and L.V.=count fingers at 3·5 metres. The left eye presents a superior coloboma, the lens being subluxated externally in the inferior part. The pupillary reflex to light persists in the right eye. The light is perceived at 4·5 m. Intra-ocular pressure in both eyes=21 mm. Blood Wassermann negative. The right eye was operated on July 1, 1932. The lens extracted after iridectomy. Its great mobility made the capsulectomy impossible. We used the cystitome and the lens was extracted with Snellen's loop. It was very flat and deep brown in colour. Post-operative course normal. Vision, with +10 D. sph. amounted to 1/8.

Case 3. I. V., aged 58 years. Entered the clinic on August 6, 1932. R.E. operated on long ago. This eye with a correction of +10 D. sph. had vision of 1/2. Left vision had been diminishing for one year. The lens had become totally opaque. Light perception was still good. Intra-ocular pressure, both eyes=16 mm. Operation on August 19, 1932, with capsulectomy. The lens was brown with greyish peripheral masses. Post-operative course normal. Vision obtained with a correction of +10 D.= 1/10.

Case 4. N. M., aged 52 years. Entered the clinic on July 6, 1935. The obscuration of the sight began in 1916, first in the right eye. For one year the patient saw nothing with this eye and only little with the left. On admission R.V. and L.V.=counts fingers at 20 cms. On slit-lamp examination one saw among the grey striations of the lens a brown colour extending through its whole thickness. Pupillary reflexes normal. Light perception for the right eye at 2·5 m. Intra-ocular pressure R.E.=18 mm., L.E.=21 mm. Blood Wassermann negative. General state good. Blood cholesterol 1·38 per cent. The right eye was operated on October 10, 1935. Extraction of the lens with iridectomy and capsulectomy. The lens was deep brown with thin greyish peripheral layers. The left eye was operated on October 16, 1935.

The lens presented the same aspect. No post-operative inflammation. On October 23 the pupil was occupied by a fine pigmentary net, so that no fundus details could be seen. Vision of the right with +10 D. correction = counts fingers at 1·5 metres. L.E. = 1/10.

In summarising these four cases we note that the age of our patients was not too far advanced (52–62 years).

Our only post-operative complication was a secondary pigmentary cataract, which is generally rare, and has been observed especially in diabetic cataract. We must point out, however, that the vision has remained reduced. This affects somewhat the prognosis of cataracta brunescens, as compared with the usual senile cataract.

Chemical Study

Our last case gave us an opportunity of studying the chemistry of the colouring substance in cataracta brunescens. The problem still remains insufficiently elucidated. We find on one side authors who could not succeed in identifying any pigment at all. Mawas, Busacca, Magnasco, Carmi, Cirincione, Neuschuller, Speciale Cirincione believe that the colour is a simple physical phenomenon due to increased refractivity of the lens. The selective absorption of shorter wave-length radiations, should thus be simply determined by the progressive sclerosis of the crystalline fibres. The majority of the authors admit however the existence of a real colouring substance, accumulating slowly in the senescent lens.

Moauro could identify once in some cases pigment of blood origin. Everybody considers to-day that the presence of such pigments is merely accidental, and unrelated to the process which determines cataracta brunescens. In some of such cases, as happened in our last case, the lens extracted from the eye was stained superficially with a drop of blood. The water in which this lens was immediately washed gave the distinct spectrum of haemoglobin. But no haematic pigment could be identified in the substance of the lens.

The recent publications of Gifford and Puntenny and of Sauermann bring new arguments to confirm the older opinion of Elschnig, Zeinek, Sliussakow, Takeishi, Rollet, Bussy, Burdon Cooper, Gatti, Nicatti, and tend to prove that pigment of cataracta brunescens belongs to the group of melanin.

The chemical composition of melanin is not yet sufficiently known. It seems to represent a group of substances, structurally very closely related. Florence and Enselme characterise melanin as: " Black pigments whose apparition is bound to a transformation *in vivo* or *in vitro* of amino-acids principally of tyrosine."

Piettre, through acid hydrolysis, obtained from melanin small amounts of tyrosine, leucine and other non-crystallisable amino-acids. Alkaline hydrolisis seems to give more alanin. Piettre has found also sulphur and even fatty chains. The action of H_2O_2 can determine the producton of small quantities of fatty acids.

Artificial synthetic melanins have been in fact obtained from tyrosine, through the action of special ferments, tyrosinases. Bloch has studied the transformation of a particular synthetic compound, the dioxyphenylalanin (dopa) under the action of a dopaoxydase, present in all places where melanogenesis takes place.

It seems, according to Rapper, that tyrosine or dopa suffer in their transformation into melanin, certain common modifications bringing to the formation of indolic rings. This correlates melanin with another amino-acid, which can result from the autolysis of proteins namely with tryptophane (acid amino-indolpropionic).

In what concerns the eye, the mechanism of production was announced by von Szily in 1911. Gatti thought to explain the brown colour of naphthalenic cataracts through an oxidation of tyrosine. Rollet, Bussy, Corrado and Nicatti have admitted the same origin for the pigment.

The condition for the production of melanin is thus the presence of two elements. A melanogenic substance of protein origin (tyrosine, dopa, perhaps tryptophane) and specific ferment tyrosinase or dopaoxidase. Whenever one of these two factors is present in a tissue we can identify it by adding the second one. The result will then be a production of melanin.

These reactions have been recently applied by Gifford and Puntenny and by Sauermann to the coloured lenses of cataracta brunescens. Gifford and Puntenny could not find any tyrosine in the lenses of cataract (senile, naphthalenic, or brunescens). Sauermann on the contrary found tyrosine and was able to detect also the presence of tryptophane in 65 per cent. of the cataractous lenses. The dopa method, which brings into evidence the oxidative melanogenic ferments, has given negative results in the cases of Sauermann and of Waelsh. Gifford and Puntenny have obtained, however, some clearly positive findings. They admit that the brown pigment is produced as a result of a slowly progressing autolysis of the lens proteins. The melanogenic amino-acids produced in the more external layers can diffuse and disappear from the lens. Only those resulting in the nuclear layers remain, and under the action of ferments similar to dopaoxydase, are transformed into pigment. Krause questions if the ultra-violet light should have also a rôle in this transformation of amino-acids into melanic substances. According to him even other amino-acids, leucin and cystine can produce melanin, whose composition is then so much more variable.

According to his own findings Sauermann thinks it is not necessary to admit the intervention of any dopaoxydase. Tryptophane is sufficiently unstable and labile to be transformed into a coloured substance without the action of such a ferment.

Burdon Cooper observes that ratio K/Ca which reaches in a normal lens 380/1 is in a cataracta brunescens 11/1 while in senile cataract only 1/1·5. He questions if K is not an activator of some melanogenic enzyme.

Previous authors studying the actual chemical behaviour of the coloured substance, had reached similar conclusions. Sliusakow thought to identify melanin through spectroscopic analysis, Takeishi through its decolouration by some characteristic bleaching agents (bromine water, chromic acid, K permanganate).

In fact the chemical identification of different pigments found in animal or vegetable bodies is quite difficult. Due to their complex and probably inconstant composition, their properties can hardly offer the possibility of classification. This has been attempted by some authors (Hueck, Vernes).

Our two brown lenses, extracted at a very short interval of days one after the other gave us an opportunity to apply these methods and to try a chemical identification of the colouring substance. One of the lenses was ground in a mortar with distilled water and the brown residue, dried, was utilised for some solubility reactions. The other lens was kept for microscopical analysis and was cut partly fresh or after fixation in formalin, and partly after paraffin embedding.

The following table gives the results of our analysis:

SOLUBILITY

KOH 3 per cent. warm	Soluble	
KOH 3 and 10 per cent. cold	Insoluble	
KOH 10 per cent. cold alcoholic	Insoluble	
NO_3H 3 per cent.	Insoluble	
C1H, CH_3COOH	Insoluble	
C1H 3 per cent. alcoholic warm	Insoluble	
SO_4H_2 conc.	Insoluble.	No colour
Water, alcohol, ether	Insoluble	
Chloroform, petroleum ether	Insoluble	
Xilol	Insoluble	
CNK 1 and 10 per cent.	Insoluble	

IRON REACTIONS

Prussian blue	Negative
Tirman Turnbull	Negative

DECOLORISING AGENTS

H_2O_2 3 per cent. and 10 per cent. ...	Negative
K permanganate 1/2000	Decoloured
Bromine water	Decoloured

BASIC DYES

Nilblue	Positive even after paraffin embedding
Neutral red	Intensely coloured before fixation and after paraffin embedding

OTHER REACTIONS

Sudan III	Negative
$AgNO_3$ Fontana	Non reduced
Dopareaction 1/1000	Negative
Nitroprusside cystine reaction	Negative
Birefringent corpuscles	Absent

Our results confirm in the first place the existence of a real colouring substance in our lenses. As Schmorl observes, colours due to simple diffraction phenomena in connection with physical structure disappear when this structure is modified. In our case colour remained unmodified by drying, pulverising, treatment with xylol and paraffin embedding. It disappeared on the contrary under the action of the usual melanin bleaching agents, bromine water and K permanganate. But as Gifford points out, the best argument is its solubility in warm (sometimes cold) KOH solutions. We have succeeded in obtaining by means of boiling in 3 per cent. KOH, a yellow solution of the colouring substance. Such solutions have been obtained by Gifford, Elschnig, Zeinek.

The whole series of reactions leads us to admit that this substance belongs really to the group of melanic pigments. In fact, the absence of any colour reaction with concentrated H_2SO_4, the lack of solubility in lipoidic solvents, exclude a carotinoid, chromolipoid nature. The absence of iron excludes the presence of blood pigments (haemosiderin). The bleaching with K permanganate excludes also the possibility of haematoidin.

Absence of malaria, insolubility in strong acid solutions, absence of double refringence plead against the presence of malaria pigment.

On the contrary all the results seem in accord with the properties of melanic pigments, except the non-reduction of $AgNO_3$. Our

pigment could not be then a real typical melanin. It could however belong to the so-called lipofuscin or " Abnützungs pigment."

Lipofuscin is found, according to Ashoff, especially in old individuals, as small yellowish to brown grains, accumulating in the cells, particularly in those of the muscles of the heart, intestines, seminal vesicles, in the epithelia of the seminal vesicles and of the pigmentary zone of the adrenal glands, testicles and other glands. In pathological conditions they are often numerous and appear especially in certain atrophic processes, giving a real macroscopic brown colour to these organs (brown atrophy of heart, liver or muscles). In the ganglial cells of the central nervous system, in the sympathetic or spinal ganglia, this pigment is found normally. It multiplies with age and in certain pathological processes can accumulate much sooner.

Recently Slatineanu, Nicolau, Balmus have found in a case of malarial coma, besides the malarial pigment, another pigment which they call " a product of metabolism " which we think belongs to the same group of substances.

Its chemical composition is not yet well-known. Salkowski thought it different from melanin. Bralen and Schmidtman on the contrary believed them related. Lubarsch considers them identical. Lipofuscin seems to be composed from a more or less constant lipoidic compound and from a melanic pigment. In opposition to melanin, it does not reduce $AgNO_3$ and accumulates just as the brown pigment of the lens slowly with the age.

According to Hueck another character which differentiates lipofuscin from melanin is its colourability in fresh, unfixed state, with 1 per cent. neutral-red solution. Lipofuscin is coloured by the basic dyes. It takes blue colour in a solution of nilblue even after treatment with lipoidic solvents, as in our case after paraffin embedding.

We must however add that even the normal lens substance has a special capacity to retain, and become stained by, histological dyes. Our normal controls were thus themselves coloured with neutral-red, so that the identification importance of this reaction is much diminished. We had the impression that the intensity with which the brown lens took, and especially retained, the dyes was distinctly greater. A section of ordinary senile cataractous lens embedded in the same block with our brown lens appears now slightly pink when the brown lens remains after one month still deeply red.

We should also mention that Kubik considered as related to lipofuscin the pigment of the Fleischer corneal ring, appearing during Wilson's hepatolenticular disease. Its real nature is just as much discussed as that of cataracta brunescens. This pigment differs however from our case through its easy solubility in KCN

Such differences could perhaps be due to real variations of composition. The inconstant presence of lipoids and perhaps of other atomic groups should give eventually different properties. The origin of lipofuscin should anyhow be (according to its name: Abnützung pigment) just as that of melanin, in the decomposition and transformation of proteins.

Cystein could bring the sulphur found in its molecule, tyrosine, eventually tryptophane should give the melanic colouring nucleus. We do not know if the ferments of the dopaoxidase type play any part in the genesis of lipofuscin.

In our case the dopareaction was negative. Even after 24 hours our sections, previously shortly fixed in formalin, presented only a homogeneous greyish tint, not different from that of the controls (ordinary senile cataract).

Bloch considers that while dopareaction and pigmentogenesis is present always in the epidermis, it takes place in the eye only in the embryonic stage or when a melanotic tumour appears. Winternitz found the tyrosine present in extracts of pig's uveal tissue. We believe that absence of tyrosine, and of tryptophane, thus of autolysis, and of the dopareaction, at the time of our research, does not exclude the possibility of melanogenesis according to the processes previously described. The long duration of time, in which the pigment accumulates only little by little proves that this process should not be intense or even continuous. As Gifford points out, the possibility of diffusion through the other layers of the lens and through its capsule, explain in part why we cannot find constantly the elements we look for.

With this we reach the last point of our discussion. All usual pigments (lipofuscin included) are found in cells in the form of grains, well individualised. In the lens of brown cataract, in our case, and in the cases of other authors (Busacca) the colour seems uniformly distributed, staining homogeneously all the fibres. Such homogeneous colouration is signalised also in the case of chloroma, where green pigment, of a nature as yet unknown, stains uniformly the cells of the tumour. This fact has not yet been pointed out in the case of melanin or lipofuscin. We must not forget however the special nature of the lens fibres. The protoplasm of cells having an active life and a complex organisation tend to isolate any foreign substance such as the pigments which accumulate and load it. It individualises them as pigmentary grains. On the contrary the fibres of the lens, through their function must assume the most homogeneous structure, and distribution of substances, in relation to the function of refraction and transparency. When treated with neutral-red it takes also a homogeneous colouration.

On the other hand, some pigmentary grains have been signalised

by some authors in cataracta brunescens. Takeishi described real grains, decolourised by oxydising agents. He considered them to be melanin grains. Gifford finds that the dopareaction shows some granulations intensely coloured in black.

It seems that the colouring substance accumulates slowly during life and diffuses homogeneously through the crystalline fibres. At the beginning they remain localised only in the nucleus and then in more rare cases occupy all the substance of the lens. As Becker has stated long since and as Vogt and Gifford pointed out again, it is very probable that between the ordinary senile yellow nucleus and cataracta brunescens, is a real transition representing the stages of the progressing processes.

Conclusions

Typical cataracta brunescens is in our practice a rare form of cataract (four cases from a total of 1,357).

Its removal presented no particular difficulties and the post-operative course was normal and devoid of any inflammatory complications. The vision has remained low, rendering therefore the prognosis somewhat inferior to that of ordinary senile cataract.

Two lenses from the same patient were chemically investigated.

A coloured substance could be extracted with hot KOH 3 per cent. All the chemical tests made, tend to prove that this substance belongs to the so-called " Abnützungs pigment " (lipofuscin).

The pigment accumulating normally with age in certain muscular, glandular or nervous cells, can sometimes appear earlier in certain pathological conditions. It seems closely related to melanin and possibly could be produced in the same way by transformation of autolytic products of proteins.

In our case the dopareaction was negative. This does not exclude however the possibility of an intermittent intervention of certain oxidative, pigmentogenic enzymes as is advanced recently by Gifford and Puntenny.

Cataracta brunescens represents probably a far advanced stage of the process which produces usually yellow senile sclerosis of the lens. As in the brown atrophy of heart and of muscles it represents the same process of accumulation of a pigment belonging to the group of lipofuscin.

BIBLIOGRAPHY

Becker.—In *Graefe-Saemisch Handb. der ges. Ophthal.*, p. 255, 1876. Quoted by Gifford.

Bloch.—In *Jadasohn. Handb. der Hautkrankheit.*, Vol. I (Springer), 1927.

Burdon Cooper.—*Trans. Ophthal. Soc. U.K.*, Vol. LIII, p. 401, 1933; *Brit. Jl. of Ophthal.*, Vol. VI, pp. 385, 483, 1922.

Busacca.—*Rev. gen. d'ophtal.*, Vol. XXXIX, p. 439, 1925. Quoted by Gifford.
Carmi.—*Boll. d'ocul.*, Vol. VIII, p. 1346, 1929; Vol. XXIII, p. 426, 1930.
Corrado.—*Arch. di Ottal.*, Vol. XXXIV, p. 201, 1927.
Cirincione.—Quoted by Gifford.
Elschnig and von Zeinek.—*Zeitschr. f. Augenheilk.*, Vol. XXIX, p. 408, 1913 Quoted by Gifford.
Florence and Enselme and Pozzi.—*Bull. Soc. Chim. Biol.*, Vol. XVII, p. 268, 1935.
Gatti.—*Ann. di Ott.*, Vol. XXXIII, p. 610, 1904. Quoted by Gifford.
Gifford and Puntenny.—*Amer. Jl. of Ophthal.*, Vol. XVI, p. 1050, 1933.
Jess.—In *Schieck and Brückner Kurzes Handb. d. Ophthal.*, Vol. CLXXXII (Springer), 1930.
Krause.—*Arch. of Ophthal.*, Vol. IX, p. 571, 1933.
Kubik.—*Klin. Monatsbl. f. Augenheilk.*, Vol. LXXXIV, p. 478, 1930.
Langeron.—Precis de Microscopie (Masson), 5th edition.
Magnasco.—*Saggi. oft.*, Vol. IV, p. 63, 1929; in *Zentralbl. f. Ophthal.*, Vol. XXIII, p. 53, 1930.
Mawas, C.—*Rend. Soc. Biol.*, Paris, Vol. CII, p. 572, 1929; *Bull. Soc. fr. Ophtal.*, Vol. XLIII, p. 3, 1930.
Moauro —Quoted by Gifford.
Neuschuller.—*Bull. Ac. Med. Roma*, Vol. LVI, p. 134, 1930; in *Zentralbl. f. Ophthal.*, Vol. XXIII, p. 789, 1930.
——— *Lett. Oftal.*, Vol. VII, 273, 1930.
Nicatti.—*Phisiol. ocul.*, Paris, 1909. Quoted by Gifford.
Rollet Bussi.—*Arch. d'ophtal.*, Vol. XXXVIII, p. 65, 1921.
Rossle.—In *Aschof Pathol. Anat.*, Vol. I, p. 322 (Fischer), 1928.
Sauermann.—*Amer. Jl. of Ophthal.*, Vol. XVI, p. 985, 1933.
Slatineanu, Nicolau et Balmus.—*Arch. Roum. de Path. exp. et microb.*, Vol. VIII, p. 5, 1935.
Sliusenkow.—In *Zentralbl. f. Ophthal.*, Vol. XXII, p. 451, 1930.
Speciale Cirincione.—*Arch. f. Augenheilk.*, Vol. LVI, p. 68, 1906.
Takeishi.—In *Klin. Monatsbl. f. Augenheilk.*, Vol. LXVI, p. 943, 1921.
Vogt.—*Arch. f. Ophthal.*, Vol. VI, pp. 108, 217, 1922.
von Szily.—*Arch. f. Mikrosc. Anat.*, Vol. LXXVII, p. 87, 1911. Quoted by Gifford.
Waelsh.—*Arch. f. Augenheilk.*, Vol. CVIII, p. 443, 1934.
Winternitz.—*Arch. f. Dermat. u. Syphil.*, Vol. CXXVI, p. 252, 1919. Quoted by Gifford.

"POSTERIOR NEEDLING" IN THE TREATMENT OF LAMELLAR AND OTHER FORMS OF SOFT CATARACT

BY

A. J. BALLANTYNE

GLASGOW

IF one may judge by the absence of all reference to it in current text books, the method of causing solution and absorption of the crystalline lens, by division of its posterior capsule, must be quite unfamiliar to at least the younger ophthalmic surgeons of the present day. I learned the operation from my seniors, and it has been practised in Glasgow for many years, both in the Eye Infirmary and in the Ophthalmic Institution, but I have been unable to trace its source.

The procedure has so much to recommend it that it would be unfortunate if it were not more widely known and practised. It is not my intention, of course, to discuss, in this place, the indications for the removal of the lens in lamellar and other forms of early cataract.

The knowledge that the substance of the lens underwent solution and subsequent absorption when exposed to the action of the aqueous humour, probably goes back to the early days of couching for cataract. It was recognised that in attempting to depress certain forms of cataract—fluid, flocculent, etc.—the needle ruptured the anterior capsule, lens matter entered the anterior chamber and its absorption followed. A slower but similar process of solution and absorption occurred in the broken lens lying in the vitreous chamber.

According to William Mackenzie, in the days of Celsus, the breaking down of the cataract into fragments by the couching needle was regarded as a proper supplementary step if displacement of the lens could not be satisfactorily performed. Barbette (1672) noticed that in such circumstances vision would be restored in seven or eight weeks. Many authors have been credited with some part in the experimental development of the discission operation (Read, 1706, Maître-Jan, 1711, Richter, 1773, Beer, 1783); but Pott (1775) and Conradi (1797) seem to have been the first to adopt it as a methodical procedure, independent of depression.

In the couching operation, the needle might be passed through the cornea and anterior chamber; or through the sclera, and between the lens and the iris, into the pupillary area, before the actual couching manoeuvre. So, in his discission operation, Conradi chose the corneal route (*Keratonyxis*) while other surgeons preferred the scleral route (*Scleronyxis*). William Mackenzie describes the operation by the scleral route under the name of *Hyalonyxis*, since the needle, having punctured the sclera about four millimetres behind the corneal margin, first enters the vitreous chamber. Its point is then turned forward and passes between the ciliary processes and the equator of the lens, then between iris and lens and into the anterior chamber, before being made to divide the capsule of the lens. In all these operations it was the *anterior* capsule which was lacerated, and the same applies to the operation as described by subsequent authors such as Weller, Travers, Pilz and others. I have found no literary reference to the operation of *posterior* needling as practised traditionally in Glasgow.

The Operation

The procedure itself is simple. The usual preparation of the eye is made and the pupil is under the influence of atropine. Anaesthesia by instillation of cocaine and adrenaline is sufficient. The

room should be darkened, and focal illumination by means of a hand lamp used. The instruments required are a speculum, fixation forceps and needle. Any sharp needle — Saunders, Knapp or Ziegler—may be employed.

The needle is passed through the sclera below the tendon of the external rectus muscle and five millimetres from the corneo-scleral junction, its point being directed into the vitreous forwards to the posterior pole of the lens. By carrying the handle of the needle backwards in the direction of the temple, the point is then turned forward and can be seen to enter the substance of the lens. A criss-cross incision is made in the posterior capsule and cortex of the lens, and the needle is withdrawn by reversing the direction of entry. Naturally, the operation occupies only a fraction of the time required to describe it. It is usual to bandage the eye for the first 24 hours, after which the bandage can be removed and the patient can move about without restriction. Atropine is continuously applied.

Opacity appears in the situation of the discission and spreads more or less throughout the rest of the lens. There is no forward swelling of the lens or shallowing of the anterior chamber. Some absorption of lens substance occurs, which apparently comes to a standstill in a week or two, and it is usual to repeat the operation after an interval of six weeks or more. The rapidity of absorption varies. Usually after two or perhaps three such needlings the lens is reduced to a thin membrane consisting of the capsule enclosing some opalescent remains of lens substance. When this stage is reached the case is completed by an anterior division of the membrane.

Advantages of the Operation

The aim of the operation is, of course, the same as that of anterior needling or discission, as usually practised, but after posterior needling it is never necessary to perform a curette extraction of the swelling lens. After anterior needling, it very occasionally happens that absorption of the dissolving lens matter keeps pace with the swelling, that the eye remains free from congestion and irritation, and that no further interference is required until a second and final needling divides the capsule and provides a clear pupil. But such a happy result is exceptional. It is impossible to pre-determine the result of a single anterior needling. Sometimes the effect is almost negligible. Again, a little opacity may appear in the lens and the process come to a standstill, apparently from closure of the capsular wound. In still other cases, the lens breaks up rapidly, masses of lens matter come forward into the anterior chamber, and the iris is pressed forward by the swelling lens.

If a curette extraction is not made at this stage, iritis or an acute rise of tension, or a combination of these two complications, may occur. This will necessitate the drawing off of the lens by linear extraction, under rather unfavourable conditions. A general anaesthetic will be necessary, and, even assuming a favourable outcome, the subsequent treatment will be somewhat prolonged. Needless to say, it will be necessary for the patient to be, from the beginning, in hospital or nursing home; a serious matter from the economic standpoint.

The uncertainties of the anterior operation and the possible occurrence of the complications referred to, are discussed in all descriptions of the operation, and most operators must have experienced some anxiety with such cases.

Contrast with this the progress of a case of posterior needling. Here too there is some uncertainty as to the result of a single needling, and it usually has to be repeated; but one can be certain that the patient will be spared the suffering incidental to the occurrence of iritis and secondary glaucoma.

From first to last there is no need for a general anaesthetic.

There is no necessity for the patient to be kept in bed. The cases may be treated as out-patients; a great gain through the saving in nursing home charges or in hospital bed accommodation. For the same reason there is little or no loss of school attendance.

Complications

The question naturally arises: Is there not a risk of detachment of the retina, owing to the site of the needle puncture? I can only recall one case in which, some years after this operation, a detachment of the retina was discovered. Assuming this to have been due to the operation, it is, so far as I am aware, unique among many scores of these cases, and no other complications have been noted. The risk seems a small one to set against the real dangers incident to the anterior operation.

Illustrative Cases

Most of my cases have been uncomplicated examples of congenital or juvenile cataract in which it was decided that the lens should be removed from one eye; but the following three more unusual cases, occur to my mind as illustrating the usefulness of the operation.

Miss B. was operated on thirteen years ago at the age of five. About a year earlier, the left eye had been operated on elsewhere with an unfortunate result. In the right eye there was a total cataract. The child was physically healthy, but her mental development was subnormal. Posterior needling was done on the left eye

on March 30, 1923, and on August 12, 1923. There was complete solution of the lens, the capsule was transparent, and no further interference was necessary. The ultimate visual result with correcting glasses was 5/5 and J.1.

Master H. W., aged 11 years, was reported to have had defective sight since birth. He had been under the care of several oculists, but no operation had been advised, chiefly because he was underdeveloped mentally and took epileptiform fits, and his family doctor considered operation inadvisable. There were dense lamellar cataracts in both eyes. The corrected visual acuity was: R. 5/36, L. 5/24, and this was not improved with mydriasis. Posterior needling was done on the right eye under a local anaesthetic on September 29, 1925, October 6, 1925, January 14, 1926, and May 14, 1926, and a final anterior division on August 24, 1926. A perfectly clear pupil was obtained, and the final visual result was 5/9 (parts) and J.1.

In these cases the good result has been maintained for thirteen and eleven years respectively, and the improved vision has had a very salutary effect on mental development.

Master D. G. was first seen in October, 1928, aged 3½ years. There was congenital dislocation of the lens, upwards in the right eye and to the temporal side in the left. Refraction was estimated with difficulty, and −8.0 D.sph. ordered for constant wear. In 1931 this was altered to − 10.0 D. giving 5/36. He was making fair progress at school, his right eye giving J.5 or 6 at very close range, but in 1934 distance vision showed some falling off, and in 1935 the left lens was found to have become opaque. It was decided to remove this lens and the posterior needling operation was done on January 2, 1936, February 8, 1936 and April 20, 1936. The lens was reduced to a small shrivelled mass below the iris at the temporal side, the pupillary area being crossed by strong zonular fibres. These were divided by anterior needling on May 16, 1936. The visual result one month later was 5/18 and J.2. No doubt this will improve. The operated (left) eye had a convergent squint in his earlier years, and the right eye was always the better seeing eye. In these cases, too, some time elapses before the full result of the operation is manifest.

Summary

The operation of posterior needling for the removal of congenital and other early cataracts is described, and its advantages indicated. Some cases are quoted to illustrate its usefulness and the results obtained.

INCIDENCE OF CATARACT AT CERTAIN AGE PERIODS IN SOUTH INDIAN DISTRICTS

BY

LIEUT.-COL. R. E. WRIGHT, I.M.S.

PROFESSOR OF OPHTHALMOLOGY, MADRAS

I HAVE have been asked frequently in the last ten years, "why is cataract so common in India?" My inclination has always been to avoid an answer, and query the inference since I had nothing very definite to go upon, in spite of the fact that in my belief cataract was exceptionally common in this country. As a rule I asked in return, "is it certain that cataract is so very much more frequent in India than in Western countries or is it largely apparently so because of the few ophthalmologists in India and the enormous population with which they deal?"

I have recently obtained some information relating to incidence which is of sufficient ophthalmological interest to record. In 1935 while conducting an enquiry into the possible aetiological influence of infra-red solar radiation on cataract production in two different areas where exposure to infra-red radiation might be expected to differ considerably, the figures referred to were revealed. Since the enquiry was conducted under the auspices of the Indian Research Fund Association and with their assistance, the full detail of it must necessarily be published in the *Indian Journal of Medical Research*. Readers of the *British Journal of Ophthalmology* (who ordinarily would not see the above publication) may find this brief extract from the data instructive.

Of 2,000 outdoor workers between the ages of 40 and 60 examined in a dry and arid district (Bellary), one person in 5·1 had cataract. Of 2,000 outdoor workers examined in a more humid and fertile area (West coast) one person in 3·4 had cataract. These figures obtained by trained observers, include of course immature cataract, even when occurring on one side only. The sexes appeared to be affected to a like extent. The apparent age was frequently given rather than the actual age since numbers of the individuals had no accurate idea of the latter. The majority probably looked older than their actual years. The figures will probably prove surprising to many.

ANNOTATION

Fireworks

The National Society for the Prevention of Blindness has sent us an illuminating table showing the number of firework accidents in connexion with the fourth of July celebrations, 1935.

The figures disclosed are staggering; a total of 6,940 injuries which were serious enough to be mentioned in the daily press. Among these were 24 deaths, 539 eye injuries and 57 cases of loss of sight. The greatest damage was among children.

Demand, of course, determines supply. We suppose that so long as fireworks are used in celebrations there will be a certain proportion of injuries. But the total disclosed in America last year is much too large and would seem to indicate the necessity of prohibiting the sale of fireworks to children altogether. Very few accidents, we believe, occur in connexion with public rejoicings in these islands, because the promoters of such festivities see that the fireworks are under the control of a responsible person. One cannot always guard against a rocket stick descending on one's head, but one should guard against small children putting their eyes out with squibs.

ABSTRACTS

I.—MEDICAL OPHTHALMOLGOY

(1) **Roy, J. N. (Montreal).—Hypertrophy of the palpebral tarsus, the facial integument and the extremities of the limbs associated with widespread osteo-periostitis: a new syndrome.** *Canadian Med. Assoc. Jl.*, June, 1936.

(1) **Roy** describes an unusual case in a man of middle age, whom he has observed for the past 10 years.

When first seen, in 1925, the man was 37 years of age. Until 15 years previously his eyelids had been normal. His work was in the manufacture of maple syrup in a forest cabin, and he was operated on about this time for chalazia. His upper lids began to feel stiff and soon became thicker than usual. At the age of 23 years he noticed that the lower lids were similarly affected. The hypertrophy of the lids has steadily progressed and has led to a bilateral ptosis.

When first seen the lids, on eversion, showed no evidence of trachoma. The conjunctiva was congested and "deep fissures nearly vertical in direction were found throughout the tarsus, giving it an irregular appearance, and separating ridges or hard nodules which had the consistence of cartilage." The conjunctiva was adherent everywhere to this hypertrophied tissue. The outer canthi were not in contact with the globes.

The lower lids were equally increased in volume, but remained in contact with the eyes. The patient complained of itching, catarrh and epiphora. The family history showed goitres in maternal grandmother, mother and three maternal aunts.

Biopsy of the hypertrophied tissue showed that the case was one of "progressive degeneration of the Meibomian glands the remains of which determined the production of foreign body granulomas, and a keloid hyperphoria of the tarsal conjunctival tissue."

The general health was good, and the Wassermann reaction negative.

Skeletal radiography showed widespread bony changes in the limbs and skull. The bones of the head showed increase in the external diameters of the skull, thickening of the vault, and enlargement of the frontal sinuses. The sella turcica was normal.

In summing up, the author states that the case presents a hyperplastic and degenerative disturbance of certain connective tissues—bones, periosteum of the long bones, skin and subcutaneous tissues of the face and extremities of the limbs, and above all, of the tarsus of the eyelids.

The paper is a long one and is illustrated by illustrations of the patient, radiograms of the forearm and skull, and microscopical sections.

R. R. J.

(2) **Schupfer (Florence).—The pathogenesis of retinitis pigmentosa. (Sulla retinite pigmentosa con particolare riguardo alla sua patogenesi).** *Boll. d'Ocul.*, February, 1936.

(2) In this long and interesting paper **Schupfer** discusses the various theories which have been suggested for the explanation of retinitis pigmentosa, and proceeds to give some account of investigations which he has made on a number of patients. He points out that recently opinion has been in favour of regarding the diencephalon and the pituitary body as probably concerned in the production of this disease. He therefore has tried to examine in his subjects the state of the functions over which these preside.

The diencephalon is that part of the brain which is derived from the second cerebral vesicle; in the adult it is barely separable from the other parts; it contains the hypothalamus and the epithalamus,

i.e., most of the structures round the third ventricle. These structures play an important part in maintaining the normal metabolism. They harmonise the workings of the various endocrine glands and control their secretions.

The author finds in all his cases some alteration of the basal metabolism, generally in the direction of increase. The function of the kidneys was altered in the majority of the patients; three showed a power of concentration definitely abnormal; four showed polyuria under the dilution test. The blood also deviated from the normal; five showed an increase in the number of the red corpuscles.

All these disorders may be attributed to disordered action of the diencephalon, but there are other changes, deafness and loss of sense of smell which cannot depend on this part of the brain. It follows that the "diencephalic theory" cannot be accepted; Schupfer points out that many of the lesions observed occur in structures derived from the mesoderm and suggests that there may be congenital changes here, which may bring about the changes in the diencephalon and thus cause retinitis pigmentosa.

HAROLD GRIMSDALE.

(3) **Giannoni and Focosi (Florence). — Recurrent vitreous haemorrhage. (Emorragie recidivanti del vitreo e diatesi emorragiche).** *Boll. d'Ocul.*, March, 1936.
Petragnani (Siena).—Recurrent vitreous haemorrhage. (Contributo all'etiopatogenesi delle emorragie recidivanti del vitreo). *Boll. d'Ocul.*, March, 1936.

(3) These two papers contain the clinical records of a number of cases of recurrent haemorrhage in the vitreous. The conclusions of the authors of the first paper are that the conditions are probably due to some alteration of the vessel walls in the direction of increased fragility; they find that recurrent haemorrhage in the vitreous is frequently associated with recurrent haemorrhage elsewhere, *e.g.*, epistaxis. The authors find that there is no evidence of tuberculosis or syphilis being in any way the cause of this disease. They find that in practically all their subjects the smaller veins were unusually fragile, as shown by bruising following light blows with a hammer over a bony surface or pinching the skin (pizzicottamento); in the latter case the bruising might not show for a day or two. They call the underlying diathesis "intermittent venous angiopsatirosis."

Petragnani, on the other hand, is inclined to allow considerable importance to tuberculosis in this disease; he finds that two out of the three individuals of whom he treats were definitely tubercular and concludes that disease of the vessels has relatively a small part in the production.

HAROLD GRIMSDALE.

(4) **Rönne, H. (Copenhagen).—Clinical studies on syphilitic choroiditis. (Klinische Studien ueber die syphilitische Choroiditis).** *Acta Ophthal.*, Vol. XII, p. 1, 1934-5.

(4) **Rönne** holds that whilst Förster's classical description of syphilitic choroiditis is still valid as a whole, appearances noted to-day differ in some detail from those in earlier days. Atrophy of the disc which Förster regarded as a constant late sign is not so frequent now and is more likely to occur in congenital than in acquired syphilis. Recurrences, too, are less frequent, and these also are more frequent in congenital syphilis. These changes he holds to be due to the earlier diagnosis and treatment of the underlying affection. The incidence of syphilitic choroiditis he found to be 2·5 per thousand in private practice and 4 per thousand in hospital practice.

ARNOLD SORSBY.

(5) **Riddell, W. J. B. (Glasgow).—The early stages of tobacco amblyopia.** *Glasgow Med. Jl.*, June, 1936.

(5) **Riddell** refers in his paper to an exhaustive investigation into tobacco amblyopia by Usher in the *Annals of Eugenics*, Vol. II, 1927, and gives his conclusions in full. The author's own case was in a man of 37 years of age who was uniocular, the other eye having been lost in the War. When first seen vision was 6/9 and J.1. He was smoking 3 ozs. of Empire tobacco a week as well as roughly 20 cigarettes a day. His daily alcoholic intake never exceeded three glasses of whisky or beer. He was advised to stop smoking and the use of spirits but was allowed to continue his beer.

The central scotoma is illustrated at various dates between October, 1933, and February, 1936.

The author's conclusions are as follow:

"The central fields have been recorded by means of small white test objects at one and two metre distances. This was found to be a satisfactory method of watching the progress. The diagrams are drawn in rectilinear co-ordinates upon squared paper. This has the advantage of saving space and is, in fact, a more accurate method than the commonly adopted one of translating a tangent screen into polar co-ordinate.

Iso-chromatic plates, such as Ishihara's, may be of great value in the diagnosis and course of this condition. Conversely, in patients with standard visual acuity, mistakes made in an iso-chromatic test may be attributed incorrectly to defective colour vision from other causes. On no occasion could this patient read Plates 10 or 11.

Tobacco amblyopia in its early stage may take two years or longer to regain normal central fields and standard colour vision. The visual acuity tested by Snellen's chart alone, may give an erroneous impression of recovery."

R. R. J.

(6) **Crisp, W. H. (Denver, U.S.A.). — Headache.** *Amer. Jl. Ophthal.*, Vol. XIX, p. 93, 1936.

(6) **Crisp** discusses the difficulties encountered in determining the pathology and aetiology of headaches. He stresses the importance of taking a broad view of a case presenting this symptom and of the necessity for the ophthalmologist to be particularly conversant with other provinces of medicine especially in oto-rhinology and neurology.

A period of post-graduate study of neurology is recommended for the ophthalmologist. Encephalitis, meningitis of slow and gradual onset, syphilitic disease of cerebral vessels are among some of the less common neurological disorders which have headaches as a principal symptom.

In assesssing other aetiological factors due weight has to be given to cardio-vascular disease, renal and gastro-intestinal disorders, endocrine allergic conditions and to the patient's psychological make up and the background of his daily life. The author states that it is well known that apart from major emotions such as fear and anger, minor emotional disturbances such as irritation, suppression, anxiety, frustration and lack of opportunity in which to do quietly some steady work are factors in inducing headaches.

In some cases where a refractive error is the cause of headache this symptom may persist in spite of wearing correcting glasses owing to failure to observe certain points in ophthalmic hygiene such as lighting, the correct posture of the head and the position of the book.

The author makes some conjectural suggestions in regard to the complex pathology of migraine and quotes Rowe who believes that some types of migraine are attributable to angioneurotic oedema of the cerebral cortex.

This paper gives an interesting survey of an important and significant symptom.

H. B. STALLARD.

(7) **Brain, Russell W. (London).—Exophthalmos following the administration of thyroid extract.** *Lancet*, p. 182, January 25, 1936.

(7) **Russell Brian** reports a case of exophthalmos following the administration of thyroid extract and discusses the sequence of events in the light of recent experimental work on the aetiology of exophthalmos.

As a rule the administration of thyroid extract or thyroxine experimentally to animals or therapeutically to man does not cause exophthalmos. Exophthalmos has occurred after partial thyroidectomy for thyrotoxicosis where thyroid extract has been given to

treat the post-operative hypothyroidism. However, this state of affairs is rare, and only some 20 cases have so far been reported in the literature.

Thyroxine or thyroid extract alone does not produce exophthalmos, but it has been thought that these substances operate synergically with a sympatho-mimetic substance, either ephedrine or ephedrone. Thyroxine appears to facilitate the action of such substance in producing exophthalmos.

The thyrotropic hormone of the pituitary is capable of producing exophthalmos in intact experimental animals, and in those who have undergone thyroidectomy, and it seems to work more readily in the presence of hypothyroidism. There is some experimental evidence to show that it acts through a nervous mechanism for excision of the superior cervical sympathetic ganglion prevents the occurrence of exophthalmos.

The author reports the case of a Jewish woman, aged 58 years, who developed exophthalmos during the administration of thyroid extract for the treatment of obesity and myxoedema.

It is probable that the exophthalmos is not the direct result of the action of the thyroid extract, but is due to another substance which in certain individuals is produced in response to the thyroid extract, and which experimental evidence suggests may be the thyrotropic hormone of the pituitary.

H. B. STALLARD.

(8) **Benedict, W. L. and Montgomery, H. (Rochester, U.S.A.)—Pseudoxanthoma elasticum and angioid streaks.** *Amer. Jl. Ophthal.*, Vol. XVIII, p. 205, 1935.

(8) **Benedict** and **Montgomery** describe eight cases of pseudoxanthoma elasticum in five of which the fundus oculi was examined. In two of these five cases angioid streaks were noted and in the remaining three the choroid was diseased, one showing evidence of degeneration and the other two post-inflammatory changes.

Gröndblad, in 1929, was the first to note the association between pseudoxanthoma elasticum and angioid streaks and in 1933 and 1934 Nomland and Klein found these two lesions associated in 19 out of 21 cases where angioid streaks were noted.

Pseudoxanthoma elasticum may begin in infancy, puberty or late in adult life. It consists in the appearance of chamois-yellow coloured nodules or papules which later become linear and may coalesce to form plaques. The adjacent skin is in lax folds. The sites of election are the folds of the neck, the axillae, inguinal region, flexures at the elbow and knees, peri-umbilical, peri-anal, the glans penis and presternal regions. Histological changes occur in the elastic tissues in the middle and deep layers of the cutis. The authors give a detailed account of these changes and discuss their nature.

In some cases it appears that the blood cholesterol, lipids, fatty acids and total lipoids show no departure from the normal whereas in others they are slightly raised.

The pathology of angioid streaks is discussed but the aetiology remains unknown. Among the conceptions that are mentioned are those of Jadassohn's who suggested that elastotoxins were the cause of the lesions; Missbildung, malformation of elastic tissue; Gröndblad, degenerative changes in the elastic layer of Bruch's membrane; and Clay, thrombosis of the posterior ciliary vessels.

H. B. STALLARD.

(9) **Appelmans, M. (Louvain). — L'Angiomatose Encéphalo-Trigéminée. Encephalo-trigeminal angiomatosio.** *Arch. d'Ophtal.*, December, 1935.

(9) **Appelmans** reports a case of encephalo-trigeminal angiomatosis affecting the areas of skin supplied by the first and second divisions of the sensory part of the left fifth cranial nerve, the left eye and the pia mater over the left side of the brain.

The patient was mentally defective, the youngest son of his family and his mother was 40 years of age when he was born.

The left eye had been removed for glaucoma. The edges of the angioma were sharply defined over the area of cutaneous distribution of the first and second divisions of the fifth cranial nerve and the neoplasm was of the simple venous variety. There were no thrills or murmurs. The affected left side of the face was less massive and less developed than the right. Radiographs of the skull showed that the vault on the left side was thicker than on the right and on its inner surface there were disseminated some irregular angiomatous dilatations spreading from the frontal to the occipital region.

The author comments that angiomata affecting one or more divisions of the trigeminal nerve and the cerebrum and its meninges are always of the simple venous variety, are congenital, and in many cases do not increase in size during life. In the case reported, the neoplasm had remained the same size since birth. He points out that the neoplasm affects the left side more commonly than the right.

Encephalo-trigeminal angioma with glaucoma is very rare. This paper contains a table summarising the literature of angiomata affecting the skin supplied by branches of the trigeminal nerve and the disorders associated with this lesion, among which are buphthalmos, glaucoma, nodules in the retina, hyperaemia of the papilla, Jacksonian epilepsy and intra-cranial involvement.

The author discusses the pathology and differentiates this type of angioma from the proliferative variety seen in von Hippel-Lindau's disease (angioblastoma) and arterial angiomata.

H. B. STALLARD.

II.—REFRACTION

(1) **Nordlöw, W.—Changes in refraction and in the capacity of horizontal movements of the eye in convergent squint of the young and in spontaneous healing. (Die Verschiebung der Refraktion und das Verhalten der horizontalen Bewegungsstreche bei Einwärtsschielern im Jugendalter sowie bei Spontanheilung des Schielens).** *Acta Ophthal.*, Vol. XII, p. 311, 1935.

(1) **Nordlöw** compares the refractions under atropine in 1,210 eyes of squinters with the curve established by Brown and Kronfeld for non squinters, and concludes that squinters show more hypermetropia. [Comparison between two racially widely separated groups is of doubtful value in refractions.—Reviewer.] Ninety-five squinters were examined after intervals of 6—7 years and the writer found that those that became rectified spontaneously showed a reduction in hypermetropia of 3·8 D.—much more than in those whose squint persisted. It is also pointed out that in squint the centre of horizontal movement is displaced inwards; the degree of movement is itself unaffected. Spontaneous rectification of the squint brought this centre back to normal, the most that persisted of this abnormality being some heterophoria. In view of a high percentage of spontaneous rectification, the author deprecates excessive operation, especially in early childhood.

ARNOLD SORSBY.

(2) **Vannas, M. (Helsingfors).—Heterophoria and depth perception. (Ueber Heterophorie und Tiefenwahrnehmung).** *Acta Ophthal.*, Vol. XIII, p. 181, 1935.

(2) **Vannas** followed up the work of Nicholson and Ask who hold that air pilots with exophoria underestimate distances whilst those with esophoria overestimate them. Inducing heterophoria by means of prisms and employing the three-rod test, Vannas found that—

(1) In exophoria, underestimations are more frequent and the errors more gross—than overestimations.

(2) In orthophoria, the same results are obtained as in exophoria, though underestimations were rather fewer and overestimates rather more. Moreover the errors were not so gross.

(3) In esophoria, underestimates and overestimates were about equal in incidence and extent.

ARNOLD SORSBY.

(3) **Heinonen, O. (Turku, Finland).—Further investigations in school myopia. (Weitere Studien ueber die Schulmyopie).** *Acta Ophthal.*, Vol. XII, p. 110, 1934-35.

(3) **Heinonen** continuing his studies in myopia reports that in elementary schools children coming from educated families show a greater incidence of myopia than those from the average population. This he holds to prove the significance of the hereditary factor in myopia, though the observation still leaves unanswered the question as to the rôle of close work in producing myopia.

ARNOLD SORSBY.

(4) **Smaltino (Naples).—The effect of the thickness of the cornea and lens on the total refractive power of the eye. (Influenze dello spessore della cornea e del cristallino sulla refrazione totale dell'occhio).** *Ann. di Ottal.*, February, 1936.

(4) As a result of calculations based on Gullstrand's schematic eye, **Smaltino** concludes that the variations of thickness of the cornea have no sensible effect on the total refractive power and that variations in the anteroposterior length of the lens are practically negligible.

HAROLD GRIMSDALE.

III.—MISCELLANEOUS

(1) **Bagghi, S.—Blindness in India.** *Calcutta Med. Jl.*, January-June, 1936.

(1) The report of **Bagghi** which runs through five numbers of the *Calcutta Med. Jl.*, is the thesis for the Jubilee Memorial Prize. It elaborates a previous paper which was noticed in an annotation last year, p. 167.

The author's summary may be abstracted here. He would arrange his cases in three groups. I. Inevitable blindness. II. Blindness, much of which might have been prevented with proper care and early treatment. III. Blindness that could have been successfully prevented by early medical aid.

In his series of cases, 307 fell into the first group, 950 into the second, and 797 into the third. He reckons that about 38 per cent. of blindness in India is absolutely preventable. He emphasises the following points in a campaign against blindness in India.

a. "Removal of illiteracy and thereby making the victim realise his loss.

b. Instructing the laity to secure proper medical aid at the right moment.

c. Stoppage of quack practice, if necessary, by legislation.

d. Provision of sufficient medical men in the villages.

e. Increasing the number of hospitals or dispensaries, properly equipped, to treat diseases of the eye.

f. Improving the social and economic condition of the children of the soil."

These various subsections are examined in more detail, and we note that the author recommends the legislature to suppress couching and to make trachoma a notifiable disease. He concludes as follows:

"In our country blindness is plentiful because ignorance, illiteracy, poverty and apathy stand as stumbling blocks in our path. . . . The fact remains that the work of prevention has never been undertaken earnestly. . . ."

R. R. J.

BOOK NOTICES

La Radiographie en Ophtalmologie. Atlas Clinique. EDWARD HARTMANN (under the auspices of the Société Française d'Ophtalmologie). Pp. 280, figures 391. Paris: Masson et Cie. Price, 230 francs.

The Société Française d'Ophtalmologie and Edward Hartmann the author of this admirable atlas of radiographs are to be congratulated on the production of so fine and valuable a piece of work.

The book is composed mainly of illustrations with explanatory legends and a certain amount of text. The author has taken considerable pains to collect together radiographs of ophthalmological interest from all over the world and it is evident that he has selected wisely from the large collection which he accumulated for the purpose of this work. The range of his task is so wide and varied that it is probable that no one ophthalmologist, however extensive his experience, would personally encounter in his clinical career examples of all the disorders shown in this atlas. The author expresses his appreciaton of the co-operation of his colleagues in this collective task.

The radiographs have been selected mainly for the characteristic features of the particular disease they illustrate and to afford the ophthalmic surgeon a work of reference so that he may compare radiographs taken in the course of his practice with those illustrated in this book.

The scope of the work is wide, chapters being devoted to radiographic evidence of general medical diseases, intra-cranial tumours and other problems of neurological interest, oto-rhinological and dental disorders and affections of the bones of the skull and face.

There are some excellent radiographs in connection with recent work on arterio-radiography showing the site of intra-cranial

aneurysms, haemangiomata and other vascular diseases after the injection of substances opaque to X-rays.

For the radiologist there are two long and interesting chapters on a number of techniques employed for the localization of intra-ocular foreign bodies and for the radiography of the optic foramen and canal. Some admirable illustrations show the value of planigraphy, the structures in the plane under examination being clearly and definitely isolated against the blurred background of other adjacent structures which would in an ordinary radiograph mask some of the features of the former. A chapter is devoted to matters of anatomical and pathological research of a radiological character, these include depth measurements of the orbit, measurement of the antero-posterior axis of the globe after the injection of diodrast into Tenon's capsule and a drop of airodol has been deposited on the centre of the cornea, thorotrast injected into the anterior chamber in the eyes prior to enucleation, angiography of the ophthalmic artery and arterio-radiography of the facial and palpebral circulation. A chapter deals with the printing of positives and an extensive bibliography accompanies the work.

The paper, printing and reproduction of the illustrations are excellent. The atlas will be very valuable both for the purpose of instruction and as a source of reference for the ophthalmic surgeon, the radiologist and the neurologist in particular.

Contribution à l'étude de la pénétration électrolytique des substances médicamenteuses dans les milieux oculaires. By MICHEL DE ROHOZINSKI. Pp. 57. Paris: E. Le François. 1936.

This monograph contains a brief review of the history of electrolysis, the laws that govern its physical and chemical operations and its therapeutic application. A chapter is devoted to the electrolytic penetration of certain medicaments; Cantonnet's work is quoted and some of his case reports have been drawn upon.

The author describes his personal experience of this method of treatment in some 30 cases 27 of which are reported. He uses the Sanion apparatus composed of 4 pocket batteries, a milliampèremetre and 2 commutators. The average current employed varies between 1 - 3 milliampères for 1 to 3 minutes. The description of the solutions is somewhat vague no details being given of the salt of the particular metal recommended and in the case reports the absence of facts concerning intervals of time between treatment and other features of interest is disappointing.

The author recommends catalysers as a useful adjuvant to the solutions employed:

The results of this therapy appear to be particularly remarkable in cases which are chronic and have resisted all other methods of

treatment. The cases reported by the author are those of chronic blepharitis, conjunctivitis, episcleritis and hyphæma.

Like Cantonnet he does not recommend the use of a local anæsthetic during the treatment, the sensitivity of the ocular tissues affording a guide to the degree of treatment the patient will tolerate.

The number of cases reported in this work is insufficient to serve more than as an indication that this branch of therapeutics deserves a trial in selected cases.

It would seem a little redundant to expend in a short work of this kind over 1½ pages on certain medicaments used in fields of general medicine other than ophthalmology.

Baillière's Synthetic Anatomy. Part XIII. Eye and Orbit. By J. E. CHEESMAN. London: Baillière, Tindall & Cox. Price, 3s.

Part XIII of this atlas of synthetic anatomy is concerned with the orbit. Some 12 plates represent the structures encountered on dissection of the orbit at progressive depths (not serial sections) in a plane slightly lateral to that of its outer wall. The enlargement is 3 times the normal size. The drawings are coloured in a distinctive and conventional manner and the structures are numbered for the purpose of reference to an index. The index is divided into sections under groups of structures such as blood vessels, muscles, nerves and so on. In some instances where the new terminology differs appreciably from the old the latter name is inserted in italics and bracketed.

The margin of every plate is divided into centimetres and marked in terms of millimetres from 0 to 170 on the short margin and 0 to 210 on the long margin. By this means it is possible to give the 'map reference' of a structure by quoting the numbers in the margins.

The atlas is well produced and affords the student a useful guide in studying the anatomy of the orbit and it gives the post-graduate a ready and attractive means of quickly revising important anatomical features in this region.

The illustrations are good and admirably planned.

Stilling's Pseudo-Isochromatic Plates for Testing Colour Perception. Edited by Geheimrat Professor DR. E. HERTEL. XIXth Edition. Leipzig: Georg Thieme. Edinburgh: F. Bauermeister, Edinburgh. Price, £1 12s. 6d.

Stilling's plates still retain their value as a preliminary test for colour blindness. In the present edition most of the older plates are retained, and others have been added. Of the latter, several adopt the excellent principle introduced by Ishihara in that they can be deciphered by typical varieties of colour blind people, but are illegible to the normal sighted. Six others adopt the principle of

Nagel's plates. The 34 plates therefore adequately fulfil all the requirements of this type of investigation.

The German text has been translated by Professor James Drever, of Edinburgh.

OBITUARY

CLAUD WORTH

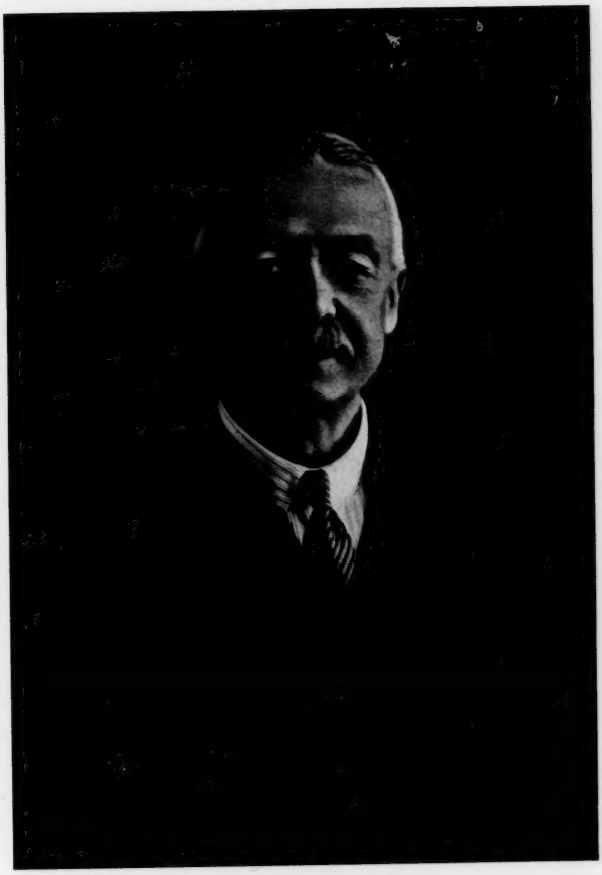
WE much regret to record the death of Mr. Claud Worth which occurred at his Cornish home on June 24. He had retired from the practice of ophthalmology for some years, meaning to devote himself to his hobby of yacht sailing, but, unfortunately, an incurable disease prevented him from accomplishing as much as he would have liked.

Worth was a Lincolnshire man, and was born at Holbeach, the son of Thomas Mordaunt Worth, representative of an ancient Lincolnshire family. He was educated at Bedford and St. Bartholomew's Hospital. He qualified as M.R.C.S., L.R.C.P. in 1893, held house-surgeonship at a hospital in the Midlands, and proceeded to the F.R.C.S. in 1898. Worth began the study of ophthalmology under Henry Power and Bowater Vernon at St. Bartholomew's and joined the practice at Moorfields, where he worked in Holmes Spicer's clinic. He was elected to the honorary staff at Moorfields in 1906 and in due course became consulting surgeon. He was, for many years, ophthalmic surgeon to the West Ham Hospital, now the Queen Mary Hospital for the East End.

His work on Squint made Worth's name familiar all over the world. His well-known book, "Squint, its causes and treatment," has reached its 6th edition and has been translated into many languages. And in the orthoptic treatment of Squint he was essentially a pioneer. Besides this he wrote a good text-book for students in conjunction with Dr. C. H. May.

Worth joined the Ophthalmological Society of the United Kingdom in 1899, and contributed many papers to its transactions. So far back as Vol. XXI he read a paper on the orthoptic treatment of Squint in Young Children. Worth's amblyoscope and "Four-light test" are part of the armamentarium of every ophthalmic surgeon, and his advancement forceps was a notable advance over the old-fashioned Prince's forceps.

Worth was very successful in handling small children. Quiet and unassuming in manner, his gentleness to his patients endeared him to young and old alike. Children instinctively trusted him.



CLAUD WORTH

But, had he not made a name for himself in ophthalmology Worth's name would have been a household word wherever yachts are sailed. His love of the sea dated from childhood, and although he was prevented from entering the Royal Navy, his knowledge of seamanship, currents, harbours and all else that go to make up the science of yachting was immense. Ten years ago he sailed his own boat to the Azores. Worth was president of the Little Ship Club, and Vice-Commodore of the Royal Cruising Club, a master mariner and first class pilot. He also wrote books on yacht sailing which are classics. In 1910, "Yacht Cruising" was published, and it has now reached its fourth edition. In 1927 he published a companion volume, "Yacht Navigation and Voyaging." Some of his boats he designed himself and he proved the practicability of sailing small boats safely in deep water; insisting that a suitable boat, manned by an efficient crew was perfectly safe, even for long voyages.

To his widow and son who survive him the sympathy of all ophthalmologists will be extended.

NOTES

Treacher Collins Memorial Fund

THE honorary treasurer of the Ophthalmological Society of the United Kingdom (Sir Arnold Lawson, K.B.E., 12, Harley Street, W.1) wishes to bring to the notice of those who still intend to contribute to this fund that the subscription list closes finally on September 30, 1936.

* * * *

North of England Ophthalmological Society.

THE President of the North of England Ophthalmological Society for Session 1936-1937 is Mr. W. H. Kiep, 33, Manor Row, Bradford. Tenure of office from October 15.

FUTURE ARRANGEMENTS

1936

October 6.—Midland Ophthalmological Society, at Birmingham Eye Hospital.

December 1.—Midland Ophthalmological Society, at Birmingham Eye Hospital.

CONTEMPORARY OPHTHALMIC LITERATURE

American Journal of Ophthalmology. *June, 1936.*

WÜRDEMANN. The formation of a hole in the macula.
ALBERS and SHEARD. The tolerance of light in exophthalmic goitre.
EDGERTON. Circinate retinitis.
BERENS. Iridocorneosclerectomy for glaucoma.
TRONCOSO and CASTROVIEJO. Microanatomy of the eye with the slit-lamp microscope.
SAMUELS. Chronic post-operative or post-traumatic retinitis (retinitis serosa).
CLARK. A case of esophoria studied by eye-movement photography.

July, 1936.

TRONCOSO and GIVNER. Megalocornea.
KRAUSE. The chemistry of the retina.
WALKER. Surgical treatment of separated retina by the galvanic method.
LAMB. The histopathology of Parinaud's conjunctivitis.
REESE. Massive retinal fibrosis in children.
TRONCOSO and CASTROVIEJO. Microanatomy of the eye with the slit-lamp microscope.
STEVENS. A method for making casts of the human cornea.
RODIN. Ptosis.

Archives d'Ophtalmologie. *July, 1936.*

WEEKERS and FANCHAMPS. Contribution to the clinical study of consensual ophthalmic reactions.
TOULANT and SARROUY. Ocular manifestations of bacillary dysentery.
PUSCARIU. Cicatrisation without ectropion with Carrel's dressing after extensive necrosis of the eyelids.
FRANÇOIS. Marginal degeneration of the cornea.

Annales d'Oculistique. *June, 1936.*

LEPLAT. Biological action of different forms of radiant energy on the ocular tissues.
WINCKLER. Double innervation of the extrinsic muscles of the eye.
SHOJI. Astigmatism of the lens.

July, 1936.

BARRAT and SEIGNER. A little known professional malady: intoxicatiom from gas proceeding from certain submarine sources where men work in diving-bells.
BUSACCA. Are nodules obtained after intra-vitreous inoculation of trachomatous material specific?

Bollettino d'Oculistica. *June, 1936.*

FIORE. The action of optochin, of fluorescein and of fluorescinated optochin on the metabolism of the pneumococcus.
NASTRI. Some effects on the eye of the local application of extracts of the posterior lobe of the pituitary.
VITO. Conjunctivitis from a wart on the free margin of the eyelid.
BORSOTTI. Contribution to the knowledge of the behaviour of the reticulo-endothelium in the repair of aseptic non-perforating wounds of the cornea.
RUBINO. A special form not previously described, of bilateral ectasia.
DE-PETRI. Contribution to the treatment of hypopyon.
HESKY. Haemostatic forceps for canthotomy.
BIOZZI. Contribution to the histological knowledge of Fuchs' heterochromia.
ROBERTO. Sclerotic protuberance in the foetal eye.

Archivos de Oftalmologia Hispano-Americanos. *July, 1936.*

BALBUENA. Connection of the rods and cones at the level of the external plexus.
ARRUGA. New pathogenic orientations and therapeutics in tabetic atrophy of the optic nerves.
CORRÉA DE BARROS. Diathermy in slight ocular hypertension.